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16. ABSTRACT

This report reviews the potential environmental hazard from the commercial use of the monohalomethanes. Chloro-, bromo-, and iodomethane are produced in commercially significant quantities; fluoromethane is produced in small amounts for use as a laboratory research reagent. The sea is a natural source of all monohalomethanes except fluoromethane. Chloromethane is used mainly for the production of silicones and tetramethyl lead (a gasoline additive). Bromomethane is used principally as a fumigant for soil, enclosed areas, and food products. Iodomethane is used as a laboratory and commercial alkylating agent and in tungsten-halogen lamps; the latter use is shared with chloro- and bromomethane. Information on physical and chemical properties, production methods and quantities, commercial uses and factors affecting environmental contamination, as well as information related to health and biological effects, are reviewed.

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a. DESCRIPTORS		b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
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methyl chloride	bromomethane	monohalomethanes	
methyl bromide	iodomethane		
methyl iodide			
fluoromethane			

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MONOHALOMETHANES

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EXECUTIVE SUMMARY

Fluoromethane, chloromethane, and bromomethane are colorless gases. Iodomethane is a colorless liquid which evaporates readily. All the monohalomethanes have faint odors. They are only slightly soluble in water.

Chloromethane, at about 411 million pounds annual production, is the most significant of the monohalomethanes from a commercial standpoint, followed by bromomethane (about 40 million pounds produced annually). Iodomethane trails a distant third at about 20,000 pounds annually. Fluoromethane is not made in commercially significant quantities; it is used in small amounts as a laboratory research reagent.

Methyl alcohol and hydrogen chloride gas are the major starting materials for the manufacture of chloromethane. Sources of bromide (hydrogen bromide or ammonium bromide) or iodide are used for the production of bromomethane or iodomethane.

Nuclear fission reactors produce radioactive iodine in the form of iodomethane. Containment of this iodomethane is not only essential because of its chemical toxicity, but also because of the potential hazard of its radioactivity. The use of halogenated pesticides and the combustion of gasoline and plants containing halogenated molecules are other activities of man which may lead to the production of monohalomethanes in the environment.

Chloromethane is used mainly as a principal ingredient for the manufacture of silicones and tetramethyl lead (an antiknock gasoline additive). Bromomethane is used mainly to kill fungi, bacteria, insects, and other pests in soil; farmhouses, boxcars, and other enclosed areas; and food products such as stored wheat, fruits, and vegetables. Iodomethane is a reactive chemical, useful in a variety of small scale commercial and laboratory chemical processes.

All of the monohalomethanes (except fluoromethane) are natural constituents of the sea and air. Algae are believed to be the main origin of monohalomethanes in the sea, from whence they diffuse into the air. Practically all the monohalomethanes monitored in the sea and air can be attributed to natural (rather than man-made) sources. Bromomethane is an exception because as much as 25% of the amount detected in the atmosphere is suspected to result from commercial sources. Monohalomethanes are removed from the environment by chemical reactions in the sea, and, as they diffuse upward in the atmosphere, by decomposition on exposure to sunlight and certain highly reactive particles in the air. Iodomethane is the least stable monohalomethane. Chloromethane and bromomethane are sufficiently stable to diffuse to the stratosphere. Fluoromethane is the most stable; if released to the environment it would probably be extremely persistent.

Chloro-, bromo-, and iodomethane are all very poisonous, with toxicity increasing in the order listed. They attack the nervous system, producing symptoms which sometimes mimic intoxication with alcohol. Often symptoms do not appear for a considerable period after the initial exposure. Periodic small exposures have been shown to result in the same type of poisoning as a single large dose. Human exposures to chloromethane are generally the result of refrigeration equipment leaks (small amounts of chloromethane are still used as a refrigerating agent). Bromomethane exposures are typically the result of poor fumigation safety practices. Recovery from less than lethal doses takes from weeks to many months, and in some cases is never complete.

Iodomethane and bromomethane are suspected of being possible cancer-causing agents. Further data are needed, however, before any of the monohalomethanes can be firmly established as carcinogens.

I. Physical and Chemical Data

A. Structure and Properties

1. Chemical Structure and Nomenclature

The monohalomethanes are derivatives of the simplest hydrocarbon, methane, CH_4, in which one of the hydrogen atoms is replaced with either fluorine, chlorine, bromine, or iodine. The standard Chemical Abstracts nomenclature for the four monohalomethanes considered in this review is listed in Table 1 along with their chemical formulas and common names.

The general terminology "methyl halide," although widespread in use, is actually misleading. These compounds do not possess the physical or chemical properties generally associated with the term "halide," which implies ionic bonding and the properties typical of metallic halides such as sodium chloride. Although the carbon-to-halogen bonds in all haloalkanes are polar (there is some charge separation due to the differing abilities of carbon and halogen atoms to attract shared electrons), the polarization never approaches the extent of charge separation of ionic compounds; the carbon-to-halogen bond is predominantly covalent in character.

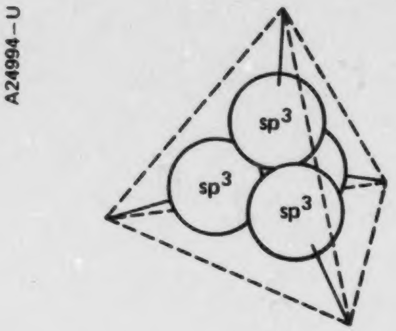
The structure and properties of the halomethanes are largely due to the nature of the parent compound, methane, and the unique characteristics of carbon chemistry. In an isolated carbon atom there are four electrons in the outer (valence) shell. These four electrons are located in two kinds of subshells or orbitals, with two electrons in an s orbital and the other two electrons in two (of three available) p orbitals. When carbon atoms combine chemically with each other or with other atoms, these nonequivalent s and p atomic orbitals change to form molecular orbitals which are fundamentally

Table 1. Monohalomethane Nomenclature

Formula	Chemical Name	Common Names
CH_3F	fluoromethane	methyl fluoride monofluoromethane
CH_3Cl	chloromethane	methyl chloride monochloromethane
CH_3Br	bromomethane	methyl bromide monobromomethane
CH_3I	iodomethane	methyl iodide monoiodomethane

different from the atomic orbitals from which they arise. In the case of four atoms bonded to a single carbon atom (i.e., methane, the halomethanes), one s and three p orbitals of the carbon atom are said to mix or "hydridize" to form four equivalent molecular orbitals which are called sp^3 molecular orbitals (Figure 1). Unlike the atomic orbitals from which they are formed, all four sp^3 hybrid molecular orbitals are energetically and geometrically equivalent and indistinguishable. They point away from the nucleus of the carbon atom, orienting themselves so as to be as far from each other as possible. Methane, therefore, is a highly symmetrical molecule whose hydrogen atoms are at the corners of an (imaginary) regular tetrahedron (Figure 1). Because carbon and hydrogen have about the same ability to attract shared electrons, the carbon-hydrogen bonds are essentially nonpolar.

With an understanding of the structure of methane and the knowledge that it is relatively inactive chemically, a great deal can be inferred about the physical and chemical properties of the monohalomethanes from the data in Table 2, obtained by experimental observation and calculations based on experimental data. The size of the halogen atoms increases in the order $F < Cl < Br < I$. As a result, the fluoromethane molecule approximates the structure of methane with a bulge due to the fluorine atom, but iodomethane approximates the structure of an iodine atom with a bulge due to the methyl group. The carbon-to-halogen distance in fluoromethane is about 30% greater than the carbon-to-hydrogen distance in methane, but the carbon-to-halogen distance in iodomethane is twice the carbon-to-hydrogen distance in methane. In order to keep the carbon-to-halogen distance within bonding range, the methyl group has to squeeze up against the halogen atom, thereby slightly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sp3
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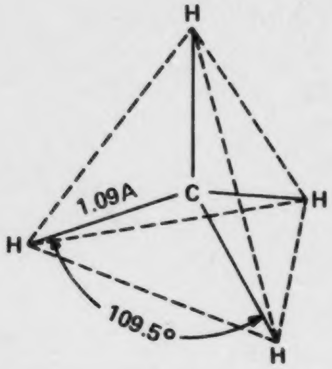
Tetrahedral sp^3 Orbitals


H
C
1.09A
H
H
109.5°
H

Shape and size showing enclosure within imaginary tetrahedron (dotted lines)

Figure 1. Methane Bond Formation and Structure (Adapted from Morrison and Boyd, 1960)

Table 2. Structural Characteristics of Methane and Monohalomethane Molecules

	C-H Bond Distance (Å)	H-C-H Angle	H-C-X Angle	CH_3-X Bond Distance (Å)	C-X Bond Energy (kcal)	C-X Bond Dipole Moment (debyes)[h]	C-X % Ionic Character[d]	Electronegativity of X[g]
CH_4	1.09^{a}	$109^{\circ}30'{}^{a}$	-	-	101^{a} (C-H)	-	7 (C-H)	2.50 (C)
CH_3F	1.0947^{c}	$110^{\circ}19'{}^{c}$	-	1.3890^{c}	107.0^{b}	1.18	35	4.10
CH_3Cl	1.090^{c}	$110^{\circ}45'{}^{c}$	-	1.781^{e}	76.7^{b}	1.85	6	2.83
CH_3Br	1.0954^{f}	$111^{\circ}38'{}^{f}$	$107^{\circ}14'{}^{f}$	1.9388^{f}	66.4^{b}	1.45	4	2.74
CH_3I	1.088^{c}	$111^{\circ}31'{}^{c}$	$107^{\circ}38'{}^{f}$	2.132^{f}	52.6^{b}	1.35	4	2.21

[a] Morrison and Boyd, 1960

[b] Glockler, 1959

[c] Eggers, 1976

[d] Calculated from the equation of Hannay and Smyth (1946) and data of Little and Jones (1960) (see text).

[e] Beltrame *et al*., 1974

[f] Kudchadker and Kudchadker, 1975

[g] Little and Jones, 1960

[h] Palmer, 1970

increasing the H-C-H bond angle and flattening the methyl group.

The carbon-to-halogen bond energies show considerable differences proceeding from C-F to C-I. The bond energy is the energy it would take to break the carbon-to-halogen bond, a measure of how easily the compound will enter into a chemical reaction. On the basis of the data in Table 2, fluoromethane should be about as chemically unreactive as methane. In fact, it is easier to remove a hydrogen atom from fluoromethane than the fluorine atom. In the case of iodomethane, however, it takes only about half the energy to break the C-I bond as compared to a C-H bond. Consequently, iodomethane should be considerably more reactive than methane or fluoromethane, and, indeed, both iodomethane and bromomethane are useful as methylating agents because of the relative weakness of their carbon-to-halogen bonds as compared to the corresponding fluoro and chloro compounds.

The % ionic character data in Table 2 was calculated from the empirical equation of Hannay and Smyth (1946) which offers a very approximate quantitative measure of the covalent or ionic character of the bond between two atoms, based on their difference in electronegativity (the tendency of an atom to attract a shared electron). The data in Table 2 show that the carbon-to-halogen bond is overwhelmingly covalent in character, although in fluoromethane it is probably best described as "predominantly" covalent. The great difference in the electronegativities of carbon and fluorine produces a highly polar bond in fluoromethane. The consequent charge separation gives rise to the minor ionic character of the carbon-to-fluorine bond.

2. Physical Properties of the Pure Material

At room temperature and normal atmospheric pressures, fluoro-chloro-, and bromomethane are all colorless gases with varying degrees of faint, characteristic odors. Bromomethane, which boils at 3.56°C, could exist as a liquid at atmospheric pressure under arctic conditions. At room temperatures and pressures pure iodomethane is a colorless liquid with a pungent odor. While the boiling points of many alkyl halides are roughly equivalent to alkanes of the same molecular weight, iodomethane is a notable exception. Its molecular weight is 142 and it boils at 42°C, whereas n-decane (molecular weight 142) boils at 176°C (Roberts and Caserio, 1964).

The haloalkanes are generally insoluble in water and very soluble in nonpolar organic solvents. Iodomethane is the most soluble of the monohalomethanes in water; fluoromethane is the least soluble. Solvolysis is achieved by the solute molecules fitting into spaces available in the solvent matrix, rather than by interaction with the solvent molecules through hydrogen bonding or becoming part of the solvent structure (Swain and Thornton, 1962). Solubility data and other physical properties relevant to this review are summarized in Tables 3 and 4. A vapor pressure/temperature curve for bromomethane is shown in Fig. 2.

Table 5 lists data for the absorption of ultraviolet light by three of the monohalomethanes. The absorption maxima, which are well below the 300 nm approximate cutoff of ultraviolet radiation at the surface of the earth, are attributed to electronic transitions from nonbonding to antibonding orbitals. Presumably any observable UV maximum for fluoromethane (which is not included in the table) would be somewhat below 170 nm according to the trend established in Table 5.

Table 3. Physical Properties of the Monohalomethanes[a]

	CH_3F	CH_3Cl[b]	CH_3Br	CH_3I[h]
Molecular Weight	34.034	50.491	94.950	141.945
Boiling Point, °C, 760 torr	-78.35	-24.22	3.56	42.5[d]
Freezing Point, °C, 760 torr	-142[j]	-97.720	-94.07	-66.1
Specific Gravity	ρ = 0.843(-60°C)[k]	0.973 (-10°C)	1.73676 (-10°C)	2.279 (20°C)[f]
Vapor Pressure, 20°C		3671.9 torr[g]	26 psia[c]	400 torr @25°C[d]
Auto Ignition Temperature, °C		632[g]	537[e]	
Odor		Characteristic, faintly sweet, ether-like[g]	At high concentrations is sweet, chloroform-like[i]	Pungent[i]
Color	Colorless	Colorless	Colorless	Colorless

[a] Anon. (1959), "Physical Properties of Chemical Compounds - II," No. 22 Advances in Chemistry Series, American Chemical Society, 1959

[b] Gallant, 1966

[c] Gallant, 1968

[d] R.S.A. Corporation, product data sheet, undated

[e] Great Lakes Chemical Corporation, Bulletin GLK128

[f] Eastman Kodak Company, product data sheet, 1976

[g] MCA, 1951

[h] Hart *et al.*, 1966

[i] MCA, 1968

[j] Downing, 1966

[k] ρ = density (Downing, 1966)

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Table 4. Solubilities of Monohalomethanes[a]

	CH_3F	CH_3Cl	CH_3Br	CH_3I
Acetone	∞	∞	∞	
Carbon Tetrachloride	∞	∞	∞	soluble
Benzene	∞	∞	∞	
Ethyl Ether	∞	∞	∞	soluble
n-Heptane	∞	∞	∞	
Ethanol	∞	∞	∞	soluble
Water	∞	5380 ppm[b]	<1000 ppm[d] (0.1 gm/100 gm)	1.4 gm/100 ml @20°C[c]

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[a] Anon. (1959), "Physical Properties of Chemical Compounds - II," No. 22 Advances in Chemistry Series, American Chemical Society (1959)

[b] Hardie, 1964

[c] Hart *et al*., 1966

[d] MCA, 1968

[e] Dilling *et al*., 1977

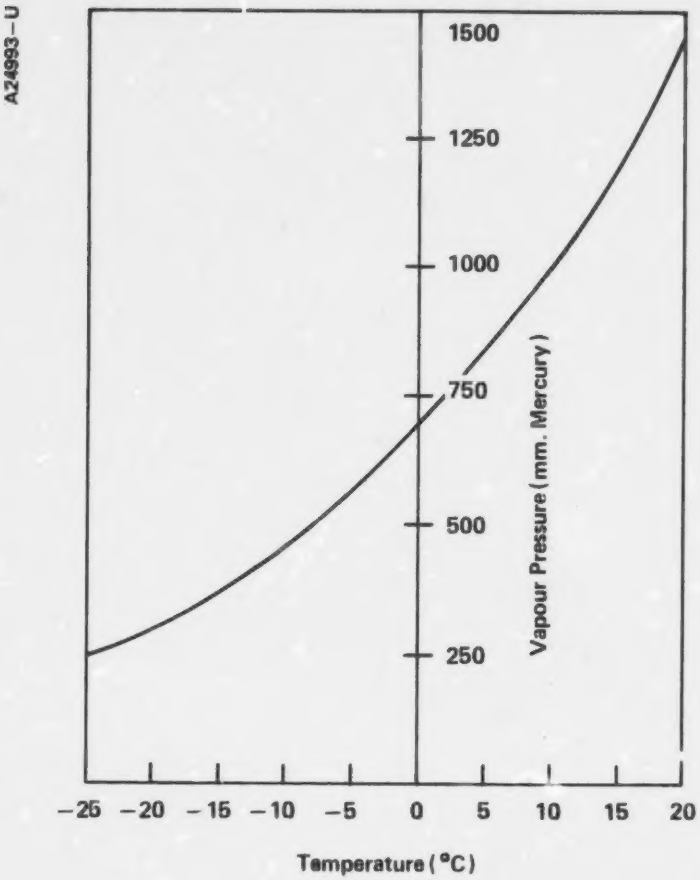


Figure 2. Vapor Pressure/Temperature Curve of Methyl Bromide (Phillips, 1963)

Table 5. Ultraviolet Absorption Data for Monohalomethanes[a]

	Type of Electronic Transition	λ_{max} (nm)	Molar Extinction Coefficient	Solvent
CH_3Cl	$n \rightarrow \pi^*$	172.5	weak	vapor
CH_3Br	$n \rightarrow \pi^*$	204.0	200	vapor
CH_3I	$n \rightarrow \pi^*$	257.5	365	pentane

[a] Roberts and Caserio, 1964

3. Properties of Commercial Material

Commercial specifications for monohalomethanes, where available, are listed in Table 6. Commercial grades of these chemicals are of high purity and the properties of the commercial materials are therefore essentially as described in the previous section. The commercial application requiring the most stringent purity standards is probably refrigeration where the aim is to produce chloromethane as completely free of moisture as possible so as to avoid hydrolysis to hydrogen chloride and consequent corrosion and early failure of the refrigeration apparatus.

4. Principal Contaminants of Commercial Products

Fluoromethane is synthesized in small quantities for research purposes. Reagent grade fluoromethane is likely to be quite pure. Probable contaminants depend on the source of the chemical and may include higher fluorinated methanes.

When manufactured by direct chlorination, chloromethane is likely to be contaminated with, in decreasing order of quantity, dichloro-, trichloro-, and tetrachloromethane. However, direct chlorination of methane accounts for less than 2% of the chloromethane currently manufactured in the United States (Blackford, 1974). Most chloromethane is made by hydrochlorination of methanol. The feedstocks are methanol and hydrogen chloride gas. The only product, besides chloromethane, is water. The most likely contaminants in the product are water vapor and hydrogen chloride gas. Depending on the intended use of the chloromethane, either or both of these can be reduced to trace amounts or less by appropriate treatment of the chloromethane prior to compression and packaging.

Table 6. Commercial Specifications for Some Monohalomethanes

	Bromomethane	Iodomethane[a]
Appearance	Colorless gas at 1 atm. and room temperature; liquid under pressure in cylinders or cans	Colorless liquid, turns brown on aging and exposure to light
Assay Purity	~100%[b]	99% min.
Specific Gravity	Liq. 1.732 @0°C ref. to water at same temp. Gas 3.27 @0°C 1 atm. ref. to air = 1	2.24 - 2.27 @25°C
Boiling Point (Range)	3.6°C	(41 - 43°C)
Refractive Index		1.526 - 1.527 @25°C

[a] Fairmount Chemical Company, product data sheet

[b] Great Lakes Chemical Corporation, personal communication

The above discussion is equally applicable to bromomethane prepared by hydrobromination of methanol, the main manufacturing method. Some bromomethane may be produced by reacting bromine and sulfur (or sulfur compounds) with methanol, in which case sulfur dioxide and/or hydrogen sulfide may be present in the product in small quantities.

Similar comments apply to iodomethane, which may be contaminated with polyiodinated methanes, or sulfur or phosphorus compounds, depending on the synthetic method employed. Iodomethane which has been exposed to sunlight or ultraviolet sources, or stored at elevated temperatures, is likely to be contaminated with decomposition products such as iodine, ethane, and iodinated ethanes.

B. Chemical Reactions in the Environment

1. Hydrolysis

The monohalomethanes hydrolyze in the presence of water to form methanol and the respective hydrogen halide. The rate of hydrolysis increases in the order fluoromethane, chloromethane, bromomethane, and iodomethane (Boggs and Mosher, 1960). The mechanism of hydrolysis is pH dependent.

The rate of a chemical reaction is usually described by an equation of the general form

$$\text{rate} = k\,\{A\}^{x}\,\{B\}^{y}\ldots$$

where $\{A\}$, $\{B\}$, and so forth represent the concentrations in moles/ℓ of the reactants and products, k is the rate constant at a given temperature, and x and y are positive numbers known as the reaction orders with respect to A, B, etc. The sum of the exponents $(x + y + \ldots)$ is called the overall reaction order. The reaction orders are zero only for those participants in the reaction whose concentration does not affect the rate of the reaction. If a set of reactions proceeds by a common mechanism (such as the hydrolysis of the monohalomethanes), the rate equations will have corresponding terms with equal reaction orders; if the concentration terms are set equal to each other, the reaction rates may then be directly compared by examining the relative values of the rate constants.

In pure water at constant pressure (no vapor phase) the monohalomethanes are slowly hydrolyzed by a reaction which is first order with respect to the halomethane (Fells and Moelwyn-Hughes, 1959) and some high order (approximately 7) (Fells, 1959) with respect to the solute. As can be seen in Table 7, activation energies for monohalomethane hydrolysis reactions are completely

Table 7. Monohalomethane Hydrolysis Data

	CH_3F	CH_3Cl	CH_3Br	CH_3I
k_1 (sec^{-1})[a]				
0°C	8.688×10^{-12}	3.20×10^{-10}	6.821×10^{-9}	8.870×10^{-10}
25°C	7.396×10^{-10}	2.353×10^{-8}	4.069×10^{-7}	7.418×10^{-8}
50°C	2.543×10^{-8}	7.552×10^{-7}	1.115×10^{-5}	2.617×10^{-6}
100°C	4.344×10^{-6}	1.318×10^{-4}	1.575×10^{-3}	5.118×10^{-4}
E_A (kcal/mole @ 100°C)[b]	22.9	26.3	25.3	26.3
$t_{1/2}$(yr) @ 25°C[c]	29.7	0.934	0.0540	0.296
k_2 ($\ell \cdot mole^{-1} sec^{-1}$)[b] for reaction with OH^- @ 100°C	8.98×10^{-4}	2.42×10^{-2}	3.52×10^{-1}	1.24×10^{-1}
E_A (kcal/mole)[b]	21.6	24.3	23.0	22.0
$t_{1/2}$ (hr)[c] @ 100°C @ pH = 8	0.173	4.66	67.8	23.9

---

[a] Heppolette and Robertson, 1959

[b] Fells and Moelwyn-Hughes, 1959

[c] Half-life calculations are based on the equation of Zepp _et_ _al_., 1975

independent of the strength of the bonds being broken. The relative reaction rates as seen in k_1 values are qualitatively what would be expected on the basis of bond energies (Table 2) for the first three compounds, but, the k_1 value for iodomethane is at least an order of magnitude less than the trend suggests it should be (Heppolette and Robertson, 1959). This may be due to the fact that the electronegativity of iodine is less than that of carbon (see Table 2), whereas the other halogens all have a much greater ability to attract a shared electron than does carbon. The carbon electron density in iodomethane should therefore be greater than in the other monohalomethanes; consequently, the carbon atom in iodomethane is less electron-deficient and more resistant to attack by species seeking centers of positive charge.

The kinetics of the neutral hydrolysis of the monohalomethanes is more complex than would be expected for simple molecules. The complexity has been attributed to the formation of a sheath of water molecules around the monohalomethane molecule; this sheath must be penetrated by the reacting species (Fells and Moelwyn-Hughes, 1959). The reacting species must also attack the monohalomethane molecule on the side opposite the halogen atom, and must therefore additionally overcome the barrier presented by the hydrogen atoms, all of which point in the direction of the approach of the reacting molecule. The further away these hydrogens are from the central carbon atom (and the further apart they are from each other), the easier it is to approach the carbon atom. Thus the reaction rate increases (k_1 values get larger, see Table 7) as the C-H bond length (Table 2) increases. Ignoring the solvent effects, however, the neutral hydrolysis of monohalomethanes may be summarized as an approximation of a monomolecular nucleophilic substitution (S_N1). The halomethane carbon atom is electron-deficient because of the electron withdrawing effect of the more electronegative halogen atom (except in the case of iodine). The carbon atom is therefore electrophilic and can attract a nucleophile (such as water) possessing a pair of electrons available for sharing. Since the rate of the reaction is dependent only on the concentration of the electrophile, the reaction order is first order (or monomolecular). An S_N1 mechanism is very unfavorable for primary halides (halogen atoms attached to the end of a carbon chain). For example, the hydrolysis of primary bromides via S_N1 is about ten times slower than for the hydrolysis of secondary bromides (such as 2-bromopropane) via S_N1. Moreover, hydrolysis of secondary bromides via S_N1 is about 10^6 times slower than tertiary bromides (e.g., 2-bromo-2-methylpropane) (Roberts and Caserio, 1964).

Kinetic calculations and laboratory experiments with sea water indicate that iodomethane reacts with chloride ion in sea water to yield chloromethane approximately as fast as the iodomethane exchanges into the atmosphere (Zafiriou, 1975). The rate of hydrolysis of iodomethane is about the same order of magnitude as the estimated exchange rate (4×10^{-7} sec^{-1}).

In addition to undergoing slow hydrolysis (Stenger and Atchison, 1964) in the presence of water, under appropriate conditions bromomethane can also form a solid hydrate with the empirical formula $CH_3Br \cdot 7.9H_2O$ (Pangborn and Barduhn, 1970). This hydrate is classed as a Type I transition clathrate crystal (modified body centered cubic lattice) with six molecules of CH_3Br and 46 molecules of water in an ideal unit cell (the experimental value of 7.9 indicates about 95% of the cells are occupied). The critical decomposition conditions for the hydrate molecule are 14.7°C and 1.51 atmospheres of pressure. Interest in this hydrate developed when its use as a desalinizing agent was suggested (see Section II-B-5). Chloromethane also forms a crystalline hydrate, $CH_3Cl \cdot 6H_2O$, which decomposes at 7.5°C and 1 atmosphere (Hardie, 1964).

At pH levels above 7, water molecules compete with hydroxide ions (which are better nucleophiles) for the electrophilic carbon atoms of monohalomethanes. As the OH^- concentration increases, the predominant overall reaction becomes

$$CH_3X + OH^- \xrightarrow{k_2} CH_3OH + X^- \quad .$$

The reaction is first order with respect to both reactants, thus second order overall; in fact, the reaction above is a classic bimolecular nucleophilic substitution (S_N2) with the solvent acting as the nucleophile. With the S_N2 mechanism, steric factors result in the following reaction rate order, with methyl halides having the highest rate: CH_3X > primary halides > secondary halides > tertiary halides. This is just the reverse of the reactivity order for the S_N1 mechanism. S_N2 mechanisms are postulated to take place in a single bimolecular step. Therefore the reactivity of a monohalomethane should be dependent upon how much energy is required to break the C-X bond. Consequently the reaction rate order for this series of compounds is $CH_3I > CH_3Br > CH_3Cl > CH_3F$ (Palmer, 1970), which corresponds to the order of the experimentally determined k_2 values in Table 7. It has been suggested (Fells and Moelwyn-Hughes, 1959) that the relatively constant k_2/k_1 ratio for this series of compounds is indicative of a consistent mechanism of hydrolysis.

Since $k_2 > k_1$ by a considerable margin, a faster rate of hydrolysis is implied for monohalomethanes in environments such as seawater, where the pH is slightly above 7, than in acidic or neutral bodies of water, where hydrolysis would be very much slower.

2. Oxidation

Saturated hydrocarbons are considerably resistant to oxidation at ordinary temperatures. Halogenated alkanes are even more resistant to oxidation (and the resistance increases rapidly as more halogen atoms are added to a molecule). The monohalomethanes therefore do not oxidize readily under ordinary conditions near the surface of the earth.

Iodomethane is considered nonflammable (R.S.A. Corp., 1977) with no effective flash point (iodomethane product data sheet, Eastman Kodak Co., 1976). Bromomethane is practically nonflammable (MCA, 1968). It also has no flash point. If exposed to intense heat, flame propagation occurs at concentrations of bromomethane between 13.5 -14.5% in air (Stenger and Atchison, 1964). Chloromethane burns feebly, but it can also form explosive mixtures with air (MCA, 1951). In contact with a flame, chloromethane burns with a white, green-edged flame, producing chiefly CO_2 and HCl (Hardie, 1964).

Oxidation of chloromethane in the troposphere has been studied by Spence et al. (1976). Although attack on chloromethane is postulated to occur primarily by hydroxyl radicals, oxidation of chloromethane was induced experimentally with chlorine atoms produced by photodissociating chlorine molecules. The proposed reaction steps are summarized:

$$Cl_2 + h\nu \rightarrow 2Cl$$

$$Cl + CH_3Cl \rightarrow CH_2Cl + HCl$$

$$CH_2Cl + O_2 \rightarrow CH_2ClO_2$$

$$2CH_2ClO_2 \rightarrow 2CH_2ClO + O_2$$

$$CH_2ClO + O_2 \rightarrow HCOCl + HO_2$$

$$HCOCl \rightarrow HCl + CO$$

The hydroperoxy radical, HO_2, can react with peroxide radicals:

$$CH_2ClO_2 + HO_2 \rightarrow CH_2ClO + OH + O_2$$

All of the chlorine eventually ends up as HCl which has a short half life in the troposphere due to being washed out by rain, but may persist for a considerable length of time in the stratosphere and take part in the ozone destruction cycle. This is further discussed in the section on environmental effects.

3. Photochemistry

In general, photolysis of monohalomethanes in the environment is limited to the upper atmosphere where ultraviolet radiation of sufficiently short wavelength (high energy) is available to initiate a reaction. The wavelength required for photolysis decreases in the order $CH_3I > CH_3Br > CH_3Cl > CH_3F$. C-X cleavage is most often observed, with the exception of fluoromethane, in which C-H cleavage is more likely (Basak, 1973). The primary cleavage products for thermal decomposition of fluoromethane are CH_2 and HF (Schug and Wagner, 1973).

Photoionization of CH_3F occurs upon irradiation with wavelengths in the range of 60-100 nm (Krauss et al., 1968). The major products are the ions CH_3F^+, CH_2F^+, CH_3^+, e^-, as well as the atoms H and F. The ionization of iodomethane is known to proceed by a loss of a nonbonding electron associated with the iodine atom (Baer et al., 1969); possibly a similar mechanism is true for the other halomethanes.

Both bromomethane and iodomethane have been used as a source of high energy ("hot") methyl radicals (Kobrinsky and Martin, 1968) formed by photolysis of the halomethane at room temperature with ultraviolet radiation of sufficiently short wavelength so the methyl radical formed has a higher kinetic energy than the average of its surroundings. These hot radicals have been used to obtain information about reaction mechanisms, such as kinetic isotope effects (Ting and Weston, 1973).

There has been more interest in the photolysis of iodomethane than any of the other compounds. It requires less energetic photons to break the C-I bond than any of the other carbon-halogen bonds, and the energy requirement is low enough so that some of these reactions occur in the lower atmosphere. The ultraviolet absorption spectrum of iodomethane is continuous from about 360 nm on down, with the first maximum about 260 nm. The primary photochemical process is

$$CH_3I + h\nu \rightarrow CH_3\cdot + I\cdot$$

At wavelengths shorter than about 315 nm, the primary process becomes

$$CH_3I + h\nu \rightarrow :CHI + H_2$$

(Tsao and Root, 1972). In the presence of oxygen, the formation of free radicals is not limited to CH_3 and I, but includes also, free radicals of oxides and peroxides such as CH_3O, CH_3O_2, CH_2O_2, HCO, and HO_2, among others. CH_3O is the most important of the oxy radicals because it undergoes disproportionation and hydrogen abstraction reactions with other radicals which result in many of the products (Heicklen and Johnston, 1962). Irradiation in the range 240-320 nm yields methanol and formaldehyde as the major products (Christie, 1958). The quantum yield of iodine atoms produced by the photolysis of iodomethane is markedly increased by the presence of small quantities of nitric oxide (NO), presumably because of the great affinity of NO for free radicals, forming in this case CH_3NO (Christie, 1959), which limits chain terminating reactions such as

$$CH_3 + I \rightarrow CH_3I$$

Irradiating aqueous solutions of iodomethane at 254 nm has the apparent effect of accelerating the hydrolysis of the halomethane. At pH 6 the main products are methanol and hydroiodic acid. Hydrolysis would normally be negligible at this pH over the period of time of the radiation (Rao et al., 1973).

Iodomethane in the solid state does not readily undergo photolysis, although longer chain alkyl halides do. At 77°K exposure to a medium or low pressure mercury lamp produces trace quantities of methane from solid iodomethane; no apparent reaction is observed at 20°K (Barnes et al., 1974).

In summary, photolysis of the monohalomethanes is likely to be a negligible process in the lower atmosphere and near the surface of the earth (with the exception of iodomethane), but may be significant in the upper atmosphere where the photolysis of monohalomethanes may affect other chemical species in the upper atmosphere (see Section III-A-2).

II. Environmental Exposure Factors

A. Production and Consumption

1. Quantity Produced

a) Fluoromethane

Fluoromethane is not produced in commercial quantities in the United States. It is only produced in small quantities for use as a laboratory reagent and other research purposes. The total volume of fluoromethane production is an insignificantly small fraction of the total monohalomethane volume on an annual basis.

b) Chloromethane

The quantities of chloromethane produced in the United States over the period 1970 - 1975 are indicated in Table 8. The current production level of chloromethane is estimated to be approximately 411 million pounds annually. Chloromethane accounts for about 90% of the total annual monohalomethane production volume in the United States.

c) Bromomethane

The quantities of bromomethane produced in the United States over the period 1970 - 1975 are indicated in Table 8. On the basis of the production trend and the fact that use of bromomethane as a fumigant appears to be increasing, the current production level of bromomethane is presumed to be approximately in the range 41-42 million pounds annually. Bromomethane accounts for about 10% of the total annual monohalomethane production volume in the United States.

Table 8. Production Volumes of Monohalomethanes 1970 - 1975*

Year	Quantities (Millions of Pounds)		
	Chloromethane	Bromomethane	Iodomethane
1975	366	36.0	
1974	493	30.0	
1973	544	29.6	0.019
1972	453	24.6	0.018
1971	437		
1970	423	21.0	0.020

Note: Missing data are not available.

*USITC, 1970 - 1975

d) Iodomethane

The quantities of iodomethane produced in the United States over the period 1970 - 1975 are indicated in Table 8. On the basis of the data and the fact that no new large bulk uses of iodomethane are anticipated, current production is estimated to be in the same range as indicated in the table, i.e., about twenty thousand pounds annually. Iodomethane accounts for about 0.01% of the total monohalomethane production volume.

2. Producers, Distributors, Importers, and Production Sites

a) Fluoromethane

The following companies can supply laboratory amounts of fluoromethane (OPD, 1976; Chemical Week, 1976):

Air Products and Chemicals
Allentown, Pennsylvania

Chemispher Corporation
Boonton, New Jersey

ICN - K&K Labs
Plainview, New Jersey

Matheson Gas Products
Lyndhurst, New Jersey

Montoco Research Products
Hollister, Florida

b) Chloromethane

The following manufacturers produce chloromethane at the indicated sites. With a few exceptions, production is concentrated in the major industrial chemical centers of the south. The total capacity of the United States to produce chloromethane is 620 million pounds annually (SRI, 1977):

	Annual Capacity (millions of pounds)
Allied Chemical Corporation	
Moundsville, West Virginia	25
Continental Oil Company	
West Lake, Louisiana	100
Diamond Shamrock	
Belle, West Virginia	25
Dow Chemical	
Freeport, Texas	70
Plaquemine, Louisiana	150
Dow Corning	
Carrollton, Kentucky	20
Midland, Michigan	15
Ethyl Corporation	
Baton Rouge, Louisiana	100
General Electric Company	
Waterford, New York	50
Stauffer Chemical	
Louisville, Kentucky	15
Union Carbide Corporation	
Institute and South Charleston, W.Va.	50
TOTAL	620

c) Bromomethane

Listed below are the producers and the production sites, together with their annual capacities, of bromomethane (SRI, 1977; CMR, 1975b; USITC, 1975):

	Annual Capacity (millions of pounds)
Dow Chemical	
Midland, Michigan	21.0

	Annual Capacity (millions of pounds)
Great Lakes Chemical Corporation El Dorado, Arkansas	27.5
Kerry McGee Trona, California	1.3
Michigan Chemical St. Louis, Michigan	5.0
Velsicol Chemical El Dorado, Arkansas	not available

d) Iodomethane

Iodomethane is manufactured by the following companies (SRI, 1977):

Columbia Organic Chemical Company
Columbia, South Carolina

Eastman Kodak Company
Rochester, New York

Fairmount Chemical Corporation
Newark, New Jersey

R.S.A. Corporation
Ardsley, New York

Imports of chloromethane are not reported separately by the Bureau of Census; however, with more than adequate production capacity available domestically and with the reasonably low selling price, it is unlikely that significant quantities of chloromethane are being imported. Imports of bromomethane are likewise not reported separately, but are very probably negligible, as 25% of the domestic production is exported (CMR, 1975b). There are no available data indicating importation of either iodomethane or fluoromethane.

3. Production Methods and Processes

a) Fluoromethane

Since there is such a small demand for fluoromethane, there has been no incentive to develop economically feasible large scale manufacturing processes. The various techniques which are available are described below.

A General Electric Patent (Cook and Wolfe, 1957) describes a novel process in which liquid hydrogen fluoride is subjected to transient electric arcs in the presence of discrete carbon particles. At low temperatures ($<$ 19°C) a number of fluorocarbons are formed. One drawback of the process is the need to separate fluoromethane from a variety of other inert compounds.

Fluoromethane can be produced in 82% yields by the decomposition of fluorosulfonic acid methyl ester (Zappel *et al*., 1963). Sulfur dioxide is also formed and makes up about 2% of the total products.

A direct electrochemical method for the partial fluorination of methane has been reported by Nagase *et al*. (1965). A bubbler type electrolytic cell is used to obtain a product, 60% of which is fluoromethane.

Hydrogen fluoride will react with formaldehyde between 100 - 680°C to form fluoromethane and difluoromethane. The product mix depends on the presence of a metal fluoride catalyst; when AlF_3 is used, fluoromethane is the sole product (Boudakian *et al*., 1968).

b) Chloromethane

Two major processes have been used to manufacture chloromethane in large quantities: direct chlorination of methane, and hydrochlorination of methanol.

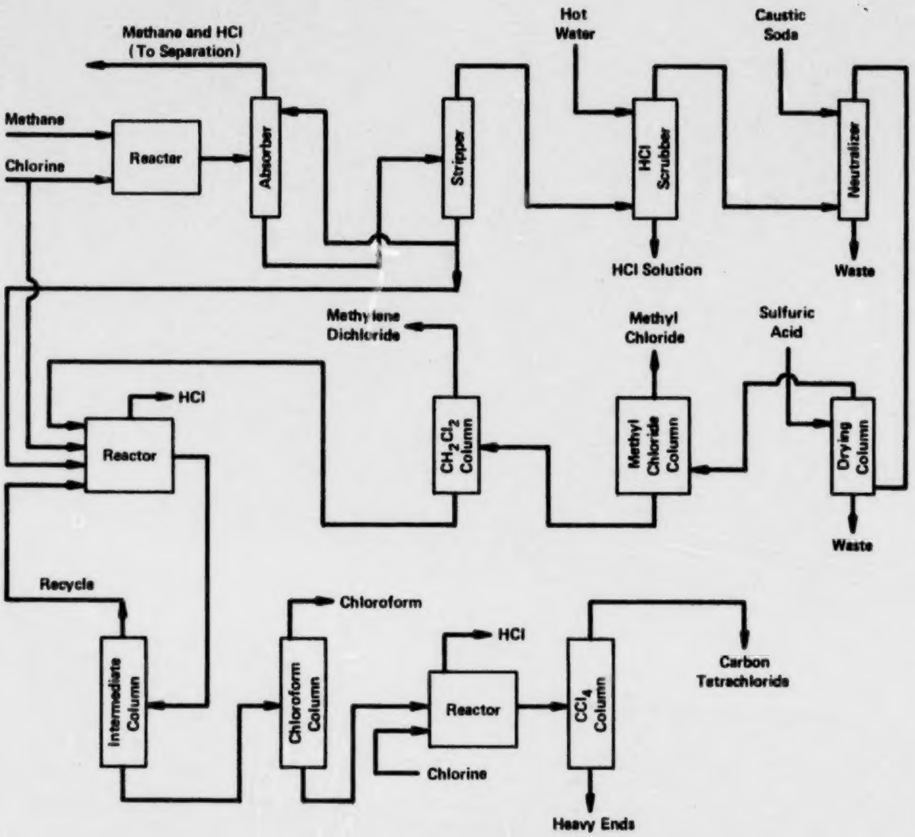
Direct chlorination of methane is a free radical chain reaction which requires light or a catalyst for induction. The overall reaction is

$$CH_4 + Cl_2 \xrightarrow{h\nu} CH_3Cl + HCl$$

The catalyst (or light) and the concentrations of reactants or products may be adjusted so that chloromethane is the major product. It is impossible to avoid producing as well, in decreasing quantities, dichloromethane (methylene chloride), trichloromethane (chloroform), and tetrachloromethane (carbon tetrachloride). This may be taken advantage of by designing a plant to recover all four products as shown in the commercial process in Fig. 3. An excess of methane in the reactor favors the formation of lower chlorinated products. The yield is 99 - 100% based on chlorine and 85 - 90% based on methane. In the process shown in Fig. 3,preheated methane (99% pure) and chlorine gases are fed to a reactor fitted with a mercury lamp. The reaction temperature is about 350 - 370°C at slightly above atmospheric pressure. Typical yields for these conditions are shown in Table 9. Effluent gases containing unreacted methane and hydrogen chloride are scrubbed with a mixture of chlorinated methanes, usually chloroform and carbon tetrachloride. The chlorinated products dissolve but the hydrogen chloride and the unreacted methane do not. A water wash separates the HCl from the methane which is recycled. The chloromethane products are separated by fractional distillation.

In 1969, 64% of all chloromethane produced in the United States was via direct chlorination of methane. In 1974, only about 2% of the chloromethane was made this way (Blackford, 1974). Direct chlorination has essentially been replaced by the hydrochlorination of methanol:

$$CH_3OH + HCl \xrightarrow{cat} CH_3Cl + H_2O$$


Methane and HCl
(To Separation)
Hot
Water
Caustic
Soda
Methane
Chlorine
Reactor
Absorber
Stripper
HCl
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HCl Solution
Waste
Methylene
Dichloride
Methyl
Chloride
Sulfuric
Acid
HCl
Reactor
CH_2Cl_2
Column
Methyl
Chloride
Column
Drying
Column
Waste
Recycle
Chloroform
HCl
Intermediate
Column
Chloroform
Column
Reactor
CCl_4
Column
Carbon
Tetrachloride
Chlorine
Heavy Ends

Figure 3. Preparation of Chlorinated Methanes by Direct Chlorination of Methane (Source: Lowenheim and Moran, 1975)

Table 9. Typical Yields for Direct Clorination of Methane*

Compound	(Common Name)	% Yield
Chloromethane	(methyl chloride)	58.5
Dichloromethane	(methylene chloride)	29.3
Trichloromethane	(chloroform)	9.7
Tetrachloromethane	(carbon tetrachloride)	2.3

---

*Lowenheim and Moran, 1975

A schematic for the process is shown in Fig. 4. Vapors of methanol and hydrogen chloride are continuously mixed in approximately equimolar ratios and passed through a preheater maintained at about 180°C. The converter stage contains a catalyst such as zinc chloride, alumina gel, or cuprous chloride, heated to 340 - 350°C, on which the reaction takes place. Calcined clay catalysts have also been successfully used (Robota and Mershon, 1975). Effluent from the converter is cooled and the chloromethane separated by fractional distillation as in the direct chlorination process (Lowenheim and Moran, 1975). The yield based on methanol is about 95%.

A variation of the method above employs an aqueous solution of methanol, hydrochloric acid, and zinc chloride, which is refluxed and distilled at 100 - 150°C to yield about 80% chloromethane (Lowenheim and Moran, 1975). Other variations including noncatalytic processes (for example, Steele et al., 1976) have been suggested.

c) Bromomethane

Phillips (1963) has reviewed the numerous processes used at one time or another to manufacture bromomethane. Direct bromination of methane is one of these. Like other alkyl halogenations, it proceeds by a free radical mechanism requiring light or a catalyst for initiation, and bromomethane is not the only product obtained; the mixture of bromomethanes must undergo extensive separation to obtain relatively pure final products.

The action of sodium, potassium, or ammonium bromides on methanol and sulfuric acid yields bromomethane of a grade suitable for use as a firefighting agent. Often the sodium bromide is of technical quality, obtained as a by-product in the manufacture of barbiturates. The methanol (99.5% + 0.5%

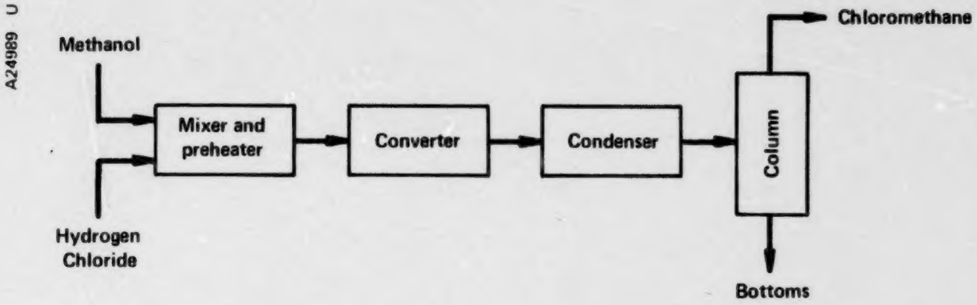
A24989 U
Methanol
Hydrogen Chloride
Mixer and preheater
Converter
Condenser
Column
Chloromethane
Bottoms

Figure 4. Manufacture of Chloromethane by Hydrochlorination of Methanol (Source: Lowenheim and Moran, 1975)

water), bromide salt, and sulfuric acid are placed in a reactor whose temperature is kept below 50°C. After a suitable period of time has elapsed the temperature is gradually raised to 90°C to expel the bromomethane, which is extracted via a water-cooled condenser at 25 - 30°C and condensed at -10°C by refrigeration and compression. Excess sulfuric acid or heat during the course of the reaction results in dimethyl sulfate contamination of the bromomethane product. Further purification is possible by redistillation. Hydrogen bromide, obtained by the relatively mild reaction of hydrogen burned in bromine gas, can be substituted for the bromide salt. The hydrogen bromide is bubbled into the methanol-sulfuric acid mixture. The yields typically obtained by this method are approximately quantitative. A schematic for the commercial production of bromomethane from methanol and bromides is shown in Fig. 5.

Another approach to the manufacture of bromomethane is the reaction of bromine with a suspension of finely divided sulfur in methanol in the presence of a small quantity of sulfuric acid at about 70°C. The sulfur acts as a reducing agent, forming hydrogen bromide, which then reacts with the methanol. The overall reaction is

$$2Br_2 + S + 4CH_3OH \rightarrow 4CH_3Br + SO_2 + 2H_2O$$

A reflux condenser returns unreacted methanol to the reaction vessel and the bromomethane is recovered by refrigeration. The yield is over 95% of theory and the product is pure enough for agricultural purposes. A pilot plant schematic adaptable to this method is shown in Fig. 6. Several variations have been proposed in the patent literature, including the use of hydrogen sulfide as the reducing agent (Yang et al., 1972), and exposing stoichiometric

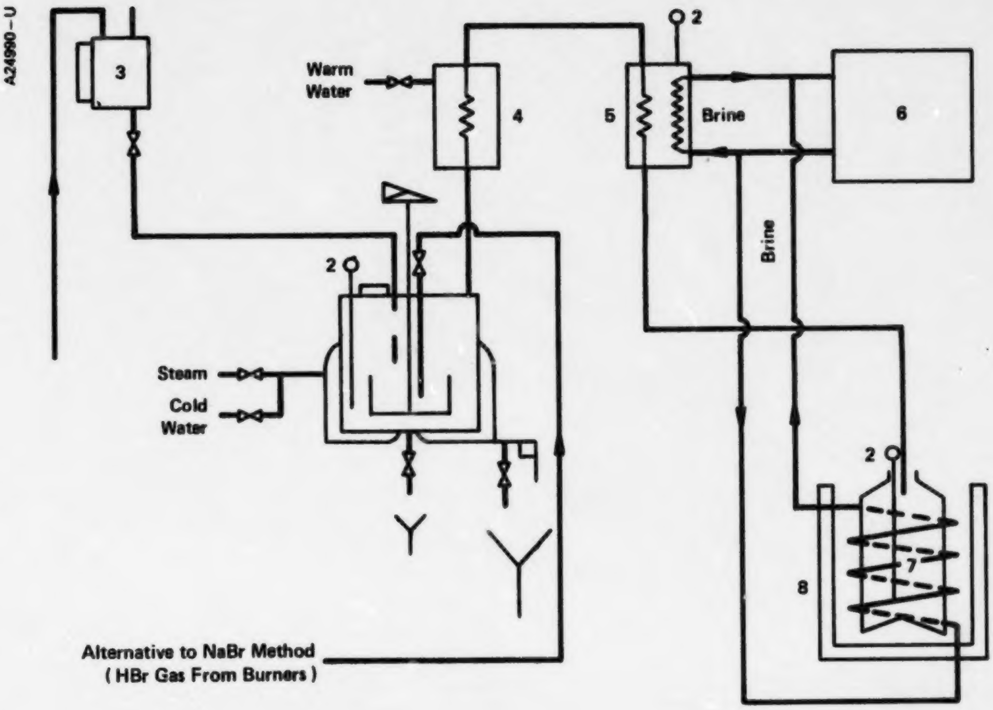
A24990-U
3
Warm Water
4
5
2
Brine
6
Brine
2
Steam
Cold Water
2
7
8
Alternative to NaBr Method (HBr Gas From Burners)

Figure 5. Bromomethane by Sodium/Potassium/Ammonium Bromide or Hydrogen Bromide Methods. Legend: (1) Reactor, (2) Thermometers, (3) Sulphuric Acid Feed, (4) Reflux, (5) Condenser, (6) Refrigerator, (7) Receiver for Bromomethane (8) Lagged Refrigerated Cold Tank (Source: Phillips, 1963)

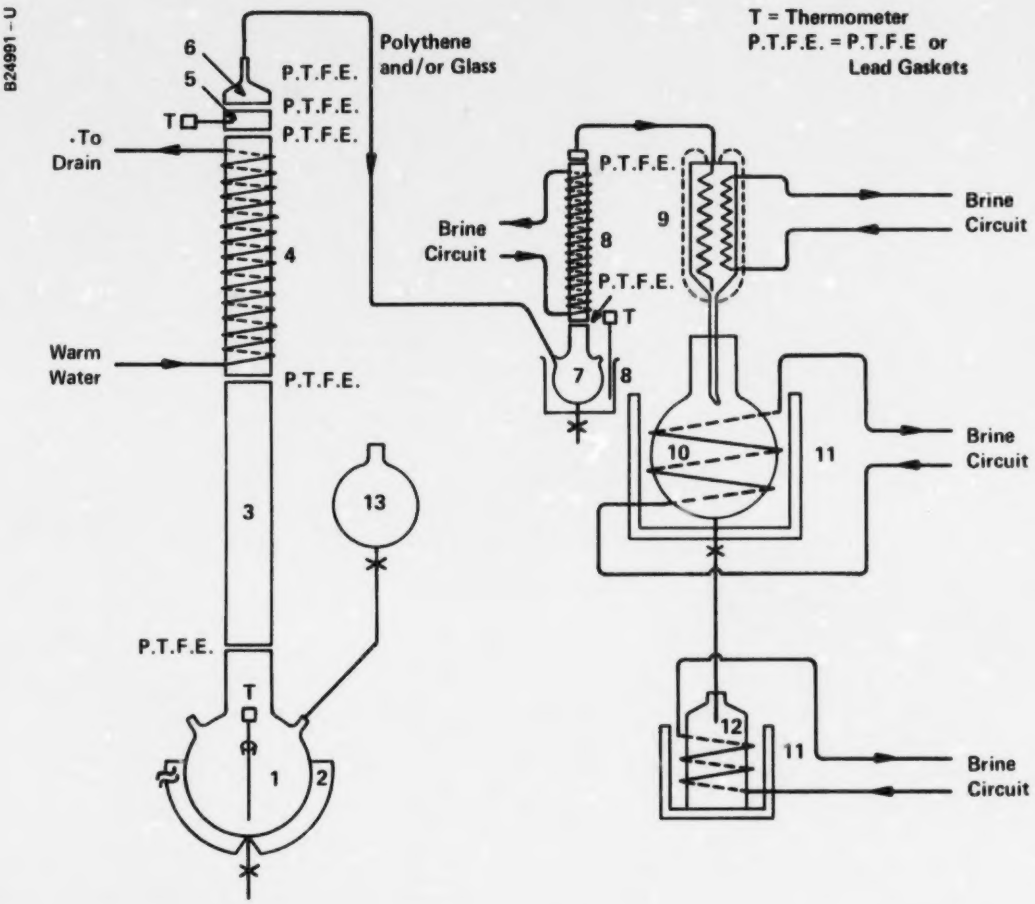
B24991-U
T = Thermometer
P.T.F.E. = P.T.F.E or Lead Gaskets
Polythene and/or Glass
6
5
T
To Drain
P.T.F.E.
P.T.F.E.
P.T.F.E.
4
Warm Water
P.T.F.E.
3
P.T.F.E.
13
T
1
2
Brine Circuit
8
P.T.F.E.
P.T.F.E.
T
7
8
9
Brine Circuit
10
11
Brine Circuit
12
11
Brine Circuit

Figure 6. Bromomethane plant for outputs of 20-30 (40-60) tons per annum, (200 ℓ.) reactor. Legend: (1) reactor, 100-200 ℓ.; (2) Isomantle, (3) copper foil packed column, (4) reflux condenser, (5) adapter for thermometer, (6) adapter, (7) methanol, etc., trap, (8) warm water bath, (9) special copper heat exchanger, (10) intermediate receiver, (11) lagged brine baths, (12) pressure bottle, and (13) feed for sulphuric acid, methanol or sulphur/bromine according to process (Phillips, 1963)

amounts of bromine and methanol to radiant energy in the ultraviolet range (Asadorian and Broadworth, 1972). The overall reaction is

$$2Br_2 + 5CH_3OH \rightarrow 4CH_3Br + 4H_2O + CO$$

d) Iodomethane

The classical method for the synthesis of iodomethane is the reaction of iodine and methanol in the presence of elemental phosphorus as a reducing agent (for example, Pico, 1971). Although iodomethane is not produced on a very large commercial scale, the desire to eliminate the hazards of the use of phosphorus and compounds such as phosphorus triiodide encouraged the investigation for alternative methods.

One of the suggested alternatives is the reduction of an aqueous solution of iodine with bisulfite ion:

$$I_2 + HSO_3^- + H_2O \rightarrow 2HI + HSO_4^-$$

The resulting hydroiodic acid is converted to iodomethane by reacting it with dimethyl sulfate:

$$HI + (CH_3O)_2SO_2 \rightarrow CH_3I + CH_3O(SO_2)OH$$

Higher alkyl iodide compounds (up to five carbon atoms) can also be prepared by this method (Huber and Schenck, 1959). Although used in the manufacture of iodomethane, one of the drawbacks of this method is that a large excess of the reducing agent (bisulfite ion) must be present at all times to avoid the reduction of sulfuric acid by HI to elemental sulfur, sulfur dioxide, and/or hydrogen sulfide. The problem can be overcome by choosing another reducing agent and keeping the pH low. A variety of reducing agents are suitable, including metals (e.g., zinc, chromium, cadmium), organic acids (e.g., oxalic, formic), certain oxides (e.g., antimony trioxide), and others (Huber and Schenck, 1962).

Iodomethane can be efficiently synthesized by gamma radiation induction of the well known free radical chain reaction between methane and iodine. The optimum conditions for maximizing the yield (60%) of iodomethane (as opposed to higher iodine substitutions) are 130°C, initial concentration of 7 mole-% iodine, and a dose rate of 8×10^{16} electron-volts per gram·minute for a total dose of 1230 rads (Vilenchich and Hodgins, 1970). Over long use, ferric iodide forms on the reactor walls, catalyzing the formation of iodomethane.

Economical commercial production of iodomethane is also achieved with an appropriate catalyst (rhodium, ruthenium, iridium, or their iodides) to cause hydrogen gas to react with elemental iodine in the presence of aqueous methanol, which results in the formation of iodomethane and water (Paulik, 1974). Alkyl iodides containing up to six carbons can be prepared by this method.

4. Market Prices

Current selling prices for commercial quantities of the monohalomethanes are listed in Table 10. Although fluoromethane is listed in the table, it is sold only in small quantities for research purposes at about $3 per gram.

5. Market Trends

The market for fluoromethane is extremely small at present and probably will not change significantly in the foreseeable future.

The recession in 1975 is blamed for the sharp decline in the production of chloromethane from 1974 - 1975. The market is expected to rebound from the low 1975 production figure at a rate of 6% per year through 1980 (CMR, 1976) because of the strong demand for chloromethane for silicones. The production of tetraalkyl leads may ease depending on the demand for unleaded

Table 10. Domestic Prices for Monohalomethanes

	Price	Reference
Fluoromethane	\$276/100 grams	ICN, 1977
Chloromethane	15¢/lb. (bulk)	CMR, 1977
Bromomethane	41¢/lb. (bulk)	CMR, 1977
Iodomethane	\$5.90/lb. (320 lb. drum)	Fairmount Chemical Co.; product data sheet

gasolines. Fig. 7 shows the capacity, production, and sales data for chloromethane from 1940 - 1975.

The production volume of bromomethane is expected to increase at a rate of 7% per year through 1979 (CMR, 1975b), reflecting a strong demand for bromomethane as a fumigant. In transport fumigation applications, the shortage of general purpose boxcars is causing railroads to assign more cars previously used for food transportation exclusively to general purpose tasks (CMR, 1975a). The change in category requires increased use of pesticides when these cars are also used to carry food products.

No significant increase in the production volume of iodomethane is expected.

Current production methods for chloro-, bromo-, and iodomethane require a readily available supply of methanol. Methanol consumption for the manufacture of chloro- and bromomethane for the years 1960 - 1973 is listed in Table 11. While current supplies of methanol are adequate for the present halomethane manufacturing demands, substantial new demands for methanol (for example, increasing its use as a gasoline constituent) could have repercussions on the supply and price of this raw material which would consequently affect the halomethane market.

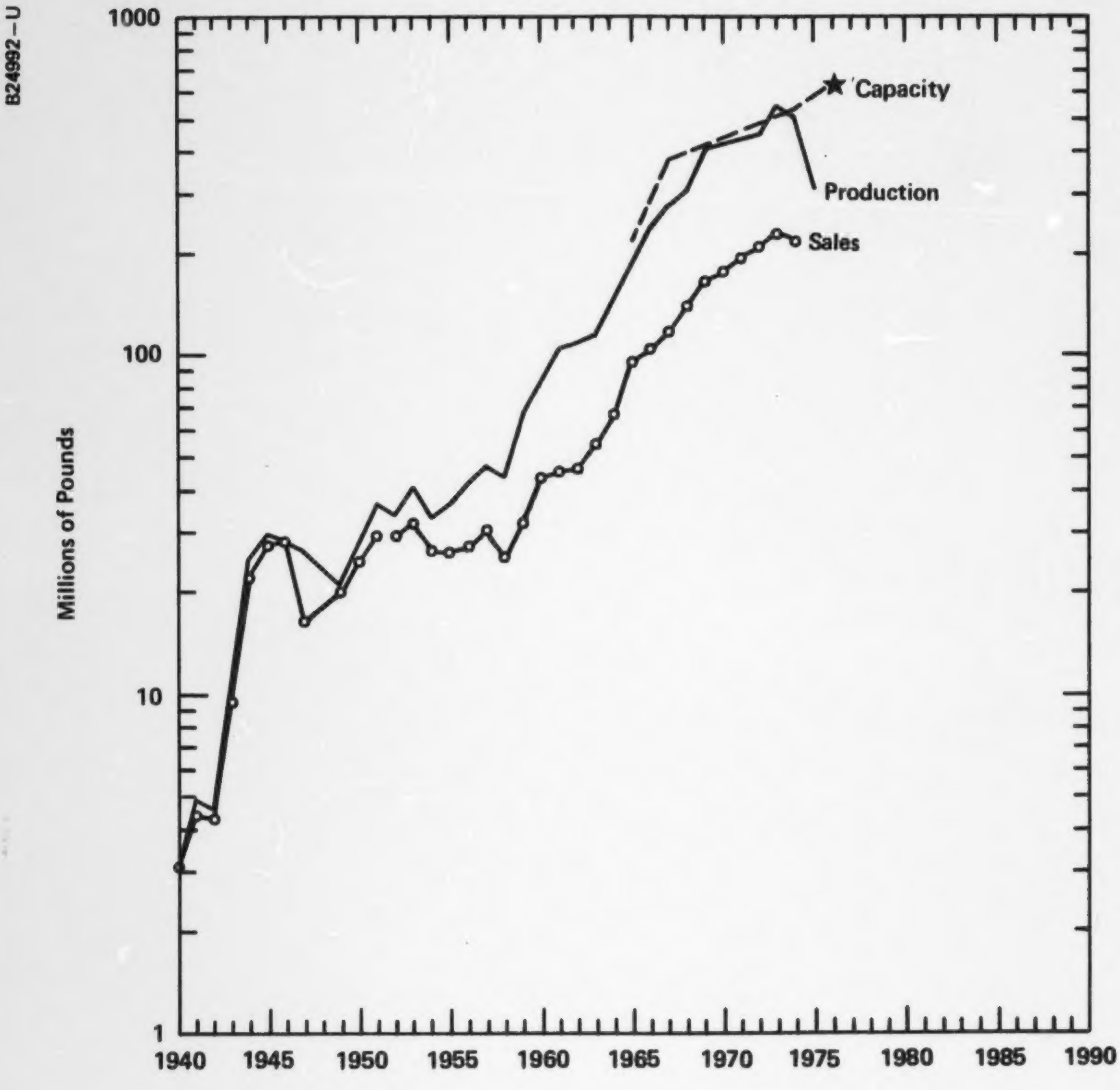

Figure 7. Market Trends for Chloromethane (Source: Blackford, 1974)

Table 11. Methanol Consumed for Monohalomethanes*

	Chloromethane (Millions of Pounds)	Bromomethane (Millions of Pounds)	Total	
			Millions of Pounds	Millions of Gallons
1960	26.3	4.7	31.0	4.7
1961	35.8	4.8	40.6	6.1
1962	44.7	4.7	49.4	7.4
1963	51.1	6.4	57.5	8.7
1964	51.0	6.3	57.3	8.6
1965	70.1	5.3	75.4	11.4
1966	106.4	6.1	112.5	17.0
1967	116.2	7.3	123.5	18.6
1968	130.8	7.6	138.4	20.9
1969	175.3	7.4	182.7	27.6
1970	204.1	7.8	211.9	32.0
1971	229.1	8.9	238.0	35.9
1972	256.0	9.1	265.1	40.0
1973	280.0	9.4	289.4	43.6

*Blackford, 1974

B. Uses of Monohalomethanes

1. Major Uses and Their Chemistry

a) Fluoromethane

There are no major commercial uses for fluoromethane. It is one of the least significant low molecular weight hydrocarbons from the commercial point of view. Its uses are discussed in the following section on the minor uses of monohalomethanes.

b) Chloromethane

Forty per cent of all chloromethane produced in the United States is consumed in the manufacture of silicones (CMR, 1976), polymers of the general formula $(R_nSiO_{(4-n)/2})_m$ where $0 \leq n \leq 3$ and $m \geq 2$ (Meals, 1969). Silicone production typically begins with the reaction of chloromethane and silicon in the presence of a copper catalyst at about 300°C. The reaction is highly exothermic. The products are methylchlorosilanes of the general formula $(CH_3)_xSiCl_y$ where $x + y = 4$. Under controlled conditions the major product is dichlorodimethylsilane (with trichloromethylsilane the chief by-product) in yields up to 95% (Meals, 1969):

$$2CH_3Cl + Si \xrightarrow{cat.} (CH_3)_2SiCl_2$$

The chlorosilane products can be separated by the usual fractionating procedures. Dichlorodimethylsilane is the starting material for the production of 91 million pounds of silicones annually (Howard et al., 1974). Chlorosilanes are converted to siloxanes by hydrolysis, followed by polymerization with acid catalysts and heat. The properties of the polymers are controlled by the reaction conditions and the addition of copolymers.

The second largest use for chloromethane is in the manufacture of tetramethyl lead, an antiknock compound widely used in gasoline formulations. There are four manufacturers of tetramethyl lead in the United States. Three of them, accounting for 95% of the tetraalkyl leads produced, manufacture tetramethyl lead by alkylating a sodium-lead alloy with chloromethane:

$$4NaPb + 4CH_3Cl \rightarrow Pb(CH_3)_4 + 3Pb + 4NaCl$$

The reaction may be catalyzed by materials such as diglyme (Newyear, 1976). A fourth company, Nalco Chemical, produces tetramethyl lead via an electrolytic procedure employing a Grignard intermediate:

$$CH_3Cl + Mg \xrightarrow{ether} CH_3MgCl$$

$$2CH_3MgCl + 2CH_3Cl + Pb \xrightarrow{elec.} Pb(CH_3)_4 + 2MgCl_2$$

The annual production of tetraalkyl leads in the United States is 890 million pounds (Bradley, 1975).

The above two uses of chloromethane account for about three quarters of the U.S. production. Four additional areas account for about 4% each:

1) In the manufacture of butyl rubber by the polymerization of isoprene at -80 to -100°C in the presence of a Friedel-Crafts catalyst, chloromethane is the usual solvent (Saltman, 1965).

2) In the industrial production of methyl cellulose, chloromethane is used interchangeably with dimethyl sulfate (Hardie, 1964).

3) Chloromethane is used in the production of certain herbicides (CMR, 1976) and to make methylmercaptan, an intermediate in the manufacture of fungicides and jet fuel additives (Hardie, 1964).

4) Chloromethane is used in the synthesis of quaternary amines (Hardie, 1964). Quaternary ammonium salts are used in the synthesis of alkenes (olefins). Other methylation reactions are discussed under minor uses of chloromethane.

Table 12 lists the major uses for chloromethane and the fraction of the production volume devoted to each use.

c) Bromomethane

The major use of bromomethane is as a fumigant to eradicate a variety of pests ranging from viral (Gammon and Kereluk, 1973), fungal, and bacterial, to insects and rodents. Fumigation uses account for 70% of the domestic production of bromomethane (25% is exported and 5% goes to minor uses) (CMR, 1975b). Table 13 demonstrates the broad range of target pests and media applicable to bromomethane treatment. The table, and the discussion which follows, are not meant to be exhaustive but rather illustrative of the diverse applications of bromomethane as a pesticide. Additional discussion of the interaction of bromomethane with biota will be found in the sections dealing with the biological effects of these compounds.

The fungicidal activity of bromomethane is well established (Munnecke _et_ _al_., 1959). It has proven to be effective with rice (Lee and Riemann, 1970) and other cereal based foods (Narasimhan _et_ _al_., 1972).

Bromomethane vapor has been shown to be bactericidal for spores of _Bactilis_ _subtilis_ and vegetative cells of _Staphlococcus_ _aureus_ and _Escherichia_ _coli_ (Jones and Phillips, 1966), as well as _Aspergillus_ _flavus_ and other members of the _Aspergillus_ genus known to infect insects likely to be found in stored food products (Srinath _et_ _al_., 1974). Bromomethane will kill

Table 12. Major Uses of Chloromethane[*]

Commercial Product	% of Production of CH_3Cl Devoted to this Use
Silicones	40
Tetramethyl lead	35
Butyl rubber	4
Methyl cellulose	4
Herbicides	4
Quaternary amines	4

[*] CMR, 1976

Table 13. Examples of Target Pests and Media for Bromomethane Fumigation

Pest	Medium	Reference
Viruses	Rice	Lee and Riemann, 1970
Bacteria (*Aspergillus* spp.)	Stored food	Srinath *et al*., 1974
Cockroaches	Ocean vessels	Ulewicz and Bakowski, 1974
Ticks (*Boophilus* spp.)	Cattle	Gladney, 1976
Coddling moth	Harvested apples	Morgan *et al*., 1974
Insects	Art works	Liberti, 1954
Insects	Poultry	Tucker *et al*., 1974
Moth larvae, beetles	Peanuts	Leesch *et al*., 1974
Insects	Human food	see text

the insects also if applied in sufficient quantity to the foodstuffs they infest (e.g., Hussein and Gouhar, 1973) or confined areas such as storage and living quarters of ships (Ulewicz and Bakowski, 1974). Bromomethane has been used to control cockroaches (Blatella germanica) (ibid.), coddling moth larve in harvested apples (Morgan et al., 1974), common dog ticks (Roth, 1973), and cattle ticks (Boophilus spp.) (Gladney, 1976).

Works of art have been rescued from destruction by insects (Liberti, 1954), and paper pests in libraries and archives eliminated with bromomethane (Waelchli, 1962).

Bromomethane is regularly applied directly to soils (1 - 2 pounds/100 sq. ft.) to eliminate fungi, bacteria, insects, nematodes, and weeds, often with a gasproof cover spread over the surface to slow the escape of the fumigant (Parris, 1958). It is sometimes combined with other fumigants which are less volatile or possess a warning odor (i.e., chloropicrin) since bromomethane vapor diluted in air is odorless, albeit highly toxic. Bromomethane appears to be especially favored in areas where cultivation is intensive, with many different crops grown and harvested in quick succession on the same soil, as in Belgium (Vanachter, 1975) or Israel (Krikun et al., 1974). The tolerance of insects to bromomethane increases significantly at lower temperatures (Bond, 1975). Therefore, the temperature of the environment to be fumigated must be taken into account in determining the amount of fumigant to be used.

Seeds appear to be more resistant than growing plants to destruction by bromomethane. A wide variety of seeds can be fumigated successfully, without affecting germination, especially under controlled low humidity conditions (Roth, 1972; Powell, 1975a).

Bromomethane is widely used in the poultry industry as a fumigant, both on chicken feed (Tucker et al., 1974) and in animal living areas. Harry and Brown (1974) have reviewed the extensive use of bromomethane in the poultry industry.

Because of its high toxicity and volatility, bromomethane has not been one of the more favored gas sterilants for food (Gammon and Kereluk, 1973), although there are many examples of its use, some of which have been noted above. The variety of foods one encounters daily for which fumigation with bromomethane (usually during storage or prior to long distance shipment) has been recommended is remarkable. Some examples include cereals (Iwata and Sakurai, 1956), oranges (Strache, 1956), coffee beans (Majumder et al., 1961), fresh fruits and vegetables (Eremenko and Spirina, 1963), mangoes (Subramanyam et al., 1969), wheat (Calderon and Carmi, 1973), peanuts (Leesch et al., 1974), cocoa beans (Asante-Poku et al., 1974), cherries (Anthon et al., 1975), and pecans (Wells and Payne, 1975), to name only a few. The growing use of bromomethane in the food industry in England prompted the Health and Safety Executive to issue a booklet advising of the hazards of its use, especially the fact that symptoms of poisoning may not appear until long after the initial exposure, resulting in the possibility of prolonged exposure (Anon., 1976a).

In addition to possibly having harmful consequences to unprotected persons exposed to bromomethane during fumigation procedures, the use of bromomethane can have an unwanted effect on the food product itself. For example, some off-flavor in candy containing fumigated nuts has been reported (Bills et al., 1969), and there is some evidence that the thiamine (Vitamin B1) content of grains may be reduced by excessive fumigation (Siesto, 1955). Thiamine also reacts with iodomethane (Okumura, 1961). (No effect on the riboflavin (Vitamin B2) content of the grains was noted in these studies.) Bromomethane is capable of methylating thiamine mononitrate at room temperature over a two month period (Okumura, 1961); however, it is very unlikely that the fumigant would ever be in contact with a food product for that length of time in normal use.

Detailed discussions of the uses of bromomethane for fumigation of soil, space, commodity, and agricultural premises can be found in the booklet "Methyl Bromide Fumigation Guide" published by the Great Lakes Chemical Corporation (Anon., undated). The booklet includes information on packaging, handling, toxicology, and emergency treatment as well as tables detailing recommended dosage and exposure times for various fumigation applications.

d) Iodomethane

The major industrial use of iodomethane is as a methylating agent (Khan _et al._, 1975), although bromomethane and even chloromethane are often preferred for this purpose because of their considerably lower cost (Hart _et al._, 1966).

Hart _et al._ (1966) reviewed a number of industrially significant reactions of iodomethane. It reacts with metals, such as lithium and magnesium:

$$2Li + 2CH_3I \rightarrow 2CH_3Li + I_2$$

$$Mg + CH_3I \rightarrow CH_3MgI$$

With amines, iodomethane gives methylamines and quaternary ammonium salts. The latter are used in the synthesis of alkenes (olefins).

$$RNH_2 + CH_3I \rightarrow RNHCH_3 + HI$$

$$RNH_2 + 3CH_3I \rightarrow R\overset{+}{N}(CH_3)_3\bar{I} + 2HI$$

Greenhalgh and Kovacicova (1975) developed a chemical confirmatory test for organophosphorus and carbamate insecticides and triazine and urea herbicides which depends on using iodomethane for methylating active NH or NH_2 moities, thus giving derivatives with gas chromatographic characteristics superior to the parent compounds. A similar technique was reported by Lawrence and Laver (1975) for some carbamate and urea herbicides. Baumgold *et al*. (1975) explained the differences in the psychotomimetic potency of a group of glycolate esters of heterocyclic amines by the different nucleophilicities of the drugs as measured by their rates of quaternization with iodomethane.

Trisubstituted phosphines react with iodomethane to yield quaternary phosphonium salts:

$$R_3P + CH_3I \rightarrow R_3\overset{+}{P}CH_3\overset{-}{I}$$

Dimethyl sulfide and dimethyl sulfoxide form complexes with iodomethane:

$$(CH_3)_2S + CH_3I \rightarrow (CH_3)_3SI$$

$$(CH_3)_2SO + CH_3I \rightarrow CH_3\overset{+}{S}O\overset{-}{I} + C_2H_6$$

Iodomethane also reacts readily to methylate unsaturated compounds, an important technique in organic syntheses. Coggins and Benoitin (1975), for example, prepared optically pure *N*-methylamino acid methyl esters in high yields using iodomethane as the methylating agent.

2. Minor Uses of Monohalomethanes

The most noteworthy application of fluoromethane has been in the development of lasers which operate in the far infrared range (Sharp *et al*., 1975; Hodges *et al*., 1976). Power output of fluoromethane lasers developed thus far has been on the order of 10 kilowatts, but lasers in the megawatt range are being planned. The fluoromethane laser exhibits a very strong laser action in the 496 μm range and has potential application in diagnostic studies of tokamak plasmas (Cohn et al., 1976).

Chloromethane is used as a solvent and blowing agent in the manufacture of some foamed plastics (Moore and Nakamura, 1967; Rodman and Andrews, 1972). Chloromethane has been used to make styrene (Kallos and Kao, 1972), acetyl chloride (Lurie, 1963), dichloromethane, chloroform, carbon tetrachloride, and various bromo- and chlorofluoromethanes (Hardie, 1964). Chloromethane is also used to make vapor pressure thermometers (Gray, 1969). Although formerly used as a refrigerant, this application of chloromethane has become much less significant, limited to certain commercial cooling units, because of its toxicity and the ready availability (up to the present) of suitable nontoxic chlorofluoroalkane substitutes. In 1963 less than 10% of the chloromethane produced in England was used for refrigeration (Hardie, 1964). Since then, that figure probably has decreased considerably.

Monohalomethanes (except fluoromethane) are used as filler gases in tungsten-halogen electric lamps (Sugano and Yuye, 1970; Johnson, 1970; Fuchi et al., 1974). These gases promote increased lamp life at brightness levels and color temperatures that are much more consistent throughout the life of the lamp than in ordinary lamps. The tungsten filament of ordinary lamps gradually evaporates as the lamp is used, coating the glass envelope with a dark filter which significantly reduces the light output and affects its spectral content. In tungsten-halogen lamps, the vaporized tungsten reacts witn the halomethane producing, at the high temperatures at which these lamps operate, tungsten halide in the vapor state. On contact with the glowing filament the tungsten halide decomposes to elemental tungsten and halogen, thus redepositing tungsten on the filament. An equilibrium develops between the rate of deposition and evaporation of tungsten, prolonging lamp life and avoiding darkening with age. Tungsten-halogen lamps are in use where reliable, high intensity light of consistent brightness and color quality is essential, including theatrical lighting, photographic studio, projection, and enlarging equipment, and certain aircraft lights.

Although bromomethane is still being used as a firefighting agent in Europe (Anon., 1976b), a replacement for it was being sought in this country as long as thirty years ago (McBee et al., 1950). Bromomethane acts to smother flames by limiting and diluting oxygen available to the fire (Creitz, 1961). In intensely hot fires, bromomethane decomposes and the bromine radicals formed react with chain carriers essential to the critical stages of combustion, removing them from the process and quenching the fire (Edmonson and Heap, 1969). Iodomethane is even more effective than bromomethane in increasing the ignition temperature of experimental propane/air mixtures (Morrison and Scheller, 1972), because the carbon-iodine bond is weaker than the carbon-bromine bond. Chloromethane and fluoromethane are, respectively, relatively less effective in preventing and extinguishing the ignition of flammable gases in air.

Table 14 lists the minor uses for halomethanes described above.

3. Discontinued Uses of Monohalomethanes

Chloromethane has largely been discontinued as a refrigerant because of its toxicity. It has been replaced by chlorofluoroalkanes (e.g., Freons^R), which are nonflammable and relatively nontoxic (as far as direct human contact with them is concerned).

Table 14. Minor Uses for Monohalomethanes

Compound	Use
Fluoromethane	Far-infrared lasers
Chloromethane	Refrigerant
Chloromethane	Foamed plastics blowing agent
Chloromethane	Polyhalomethane synthesis
Chloromethane	Solvent and reagent in chemical manufacturing
Chloromethane	Tungsten-halogen lamps
Bromomethane	Tungsten-halogen lamps
Bromomethane	Fire-extinguishing agent
Iodomethane	Tungsten-halogen lamps

Bromomethane has been abandoned as a firefighting agent in this country, because, like carbon tetrachloride, it is toxic and hazardous to work with.

4. Proposed Uses for Monohalomethanes

Chloromethane (Glew, 1962) and bromomethane (Barduhn et al., 1960) have been proposed for use as desalinizing agents because they form hydrates with a high ratio of water to halomethane (see section I.B.1, p. 15). The problem of residual halomethane in the desalinized water makes this approach unattractive with present technology.

Fluoromethane has been proposed as a propellant fuel in combination with F_2O as an oxidizer for large rocket engines (Kanarek, 1961). CH_3F and F_2O can be safely mixed, handled, and stored at ambient temperatures, eliminating the need in the rocket for separate storage chambers, pumps, etc. for fuel and oxidizer. The mixture can also be used regeneratively to cool the rocket engine, as is the practice with dual fuel/oxidizer systems.

5. Alternatives to Uses for Monohalomethanes

In its use as a mild alkylating agent, chloromethane can be replaced by a variety of chemicals. Fluoromethane and iodomethane are not used on a wide enough scale to be concerned with replacing them.

Most of the other chemical uses for monohalomethanes depend on the unique and specific properties of the compound. While one of these compounds may replace, or even be interchangeable, with another for certain applications, as a general rule it is not likely that replacements can easily be found which will not present environmental problems of some sort themselves.

Consider the replacement of chloromethane by chlorofluoromethanes as refrigerants. While the latter lack the toxic properties of the monohalomethane, they may present subtle but significant environmental hazards of their own (e.g., stratospheric ozone destruction).

The use of bromomethane as a fumigant is an exception to the above generalization. Bromomethane is only one of a myriad of halogenated hydrocarbons, carbamates, organophosphates and other compounds which can be used for pest extermination and sterilization. It has, however, a number of desirable properties which are not necessarily shared by these others; it penetrates thoroughly, obviating the need for opening crates and containers which are not airtight (e.g., jute bags), and it dissipates rapidly, becoming undetectable in a matter of days. These properties are, of course, shared by iodomethane, which has been suggested as a substitute fumigant for bromomethane because iodomethane is easier to handle, being a liquid (Muthu and Srinath, 1974; Muthu et al., 1976). Probably more desirable than replacing bromomethane with another toxic chemical would be the use of entirely different techniques to achieve the same results. Live steam, for example, has been shown to be superior to bromomethane in preventing the spread of mushroom virus disease (Dieleman-van Zaayen, 1971). Microwaves can replace bromomethane fumigation of soil in a method developed by the Oceanography International Corporation (Anon., 1973). In a portable machine called a Zapper, electricity from a 155 kilowatt diesel generator is converted by klystron tubes into microwave radiation which can penetrate the soil to a depth of 24", killing weeds as well as fungi, nematodes, insects, etc. In use, a Zapper leaves no toxic residues and there is no pollutant runoff. It is said to be economically viable wherever weed control exceeds $15/acre (in 1973) and has been demonstrated with a pepper crop in North Carolina.

C. Environmental Contamination Potential

1. General

The three monohalomethanes which are produced in commercially significant quantities are also natural constituents of the oceans and atmosphere. Their presence in the environment is therefore obviously tolerable at the natural background levels, and the problem is to determine if there is an additional sustainable load without significant environmental alteration. Monitoring studies such as those conducted by Lovelock et al. (1973), Grimsrud and Rasmussen (1975), and Singh et al. (1977) are an essential step in this direction.

Monohalomethanes are volatile chemicals which have the potential for being dispersed if they are not properly contained. However, with the exception of bromomethane, all the monohalomethanes are produced, transported, and used in closed systems. All the compounds except fluoromethane have been detected in the environment but most of the quantity detected has been attributed to natural sources.

2. From Production

The hydrochlorination of methanol is a straightforward chemical process with little opportunity for environmental contamination other than through leaks in storage or holding tanks or pipelines. This is more than a passing possibility because of the pressures required to compress and liquify chloromethane gas. The high yield of chloromethane (95%) and recirculation of unreacted starting materials (methanol and hydrogen chloride) minimizes their opportunity for escape. Replacement of the catalyst and/or cleaning of the reactors would provide the most likely source of release of chloromethane to the atmosphere.

The hydrobromination of methanol to produce bromomethane can be accomplished in a variety of ways, but the general processes and procedures are similar to the manufacture of chloromethane. Therefore, the same comments made above with respect to storage and holding tanks and pipelines apply to bromomethane. Refrigeration systems may be substituted for high pressure in the containment of liquid bromomethane as it boils at about 38°F. In addition to leaks of bromomethane from production, packaging, or storage areas, certain processes used to make the bromomethane form by-products which are potential environmental contaminants should they be discarded through stacks to the atmosphere. For example, those processes employing sulfur or sulfur compounds produce sulfur-containing by-products such as sulfur dioxide. The direct reaction of bromine and methanol in the presence of ultraviolet radiation also yields carbon monoxide.

The manufacture of iodomethane is technologically similar to bromomethane, but since only about 1/2 pound of iodomethane is produced for every 1,000 pounds of bromomethane, the potential for environmental contamination from commercially produced iodomethane is relatively insignificant.

3. From Transport and Storage

Fluoromethane and chloromethane must always be shipped and stored in pressurized containers. There is always a potentially serious hazard associated with transporting and storing any substance under pressure, particularly a toxic substance. This is illustrated by an accident which occurred near Gretna, Florida, in August, 1971 (Anon., 1972). A truck and an automobile collided on U.S. 90. The truck was of the tractor-van type semi-trailer bearing a cargo of steel cylinders containing a mixture of bromomethane and chloropicrin pressurized with air. (It is not necessary to ship bromomethane under pressure if refrigerated equipment is available, as it will not boil below about 38°F.) Several of the steel cylinders, which were unsecured, came loose during the crash. One of these, sustaining a broken "fail-open" valve, landed on top of the automobile. The day was hot and humid and the air was still. Escaping bromomethane filled the automobile and four disabled passengers in it died of bromomethane intoxication. The National Transportation Safety Board attributed the severity of the losses to, among other factors, failure of the carrier to secure the bromomethane cylinders, the pressurization of the cylinders, and the type of valve in use on the cylinders.

No mishaps have been reported for the other monohalomethanes. The quantities of monohalomethanes lost during transport and storage are likely to be small.

4. From Use

There is no significant environmental contamination potential perceptible at this time from the use of fluoromethane, since it is produced in such small quantities and its uses are restricted to research purposes.

More than 90% of the chloromethane produced in this country is used as a reagent in other chemical processes (see Table 12), and is therefore not available to enter the environment. Certain minor uses, such as a solvent or blowing agent in the manufacture of foamed plastics, have the potential for hazardous exposure and possible escape to the atmosphere. Some pesticide formulations use chloromethane as a solvent and propellant. Such use places chloromethane directly into the atmosphere, and if used near food, especially fatty food, it can get into the food. Like bromomethane, chloromethane tends to persist in fatty foods for many days after the initial exposure.

The major opportunity for environmental contamination with bromomethane comes with its use as a fumigant. It thereby gets into soil, food, and the air, and presents a potentially serious hazard to the applicators during the period of fumigation. It can affect food products (e.g., discolor wheat) (Brown and Jenkinson, 1971), and tends to raise the bromide ion concentration in fumigated food products (e.g., Van Wambeke, 1974; Hoffman and Malkomes, 1975); the resident time of bromomethane itself, however, is generally limited to a day or two in foods, except fatty foods (such as nuts) (Desbaumes and Deshusses, 1956) or soil (residence time is depth-dependent) in which it may persist for three to six weeks.

Plonka has estimated that 25% of the industrially produced bromomethane is released to the atmosphere (Wofsy et al., 1975), which led Wofsy et al. (1975) to conclude that perhaps from 5 - 25% of the bromomethane in the atmosphere is traceable to anthropogenic sources. A possible source suggested by Wofsy et al. (1975) (other than fumigation) is the formation of bromomethane from dibromomethane during the combustion of leaded gasoline.

Bromomethane may present some hazards, other than its toxicity, in certain industrial and laboratory reactions. An explosion has been reported involving the reaction of bromomethane and dimethyl sulfoxide to produce trimethylsulfoxonium bromide (Scaros and Serauskas, 1973). Synthetic uses for bromomethane account for a minor amount of its consumption.

The major environmental contamination potential for iodomethane is during its use as an alkylating agent in chemical laboratories and use may result in human contact. Some human exposures in chemical laboratories have resulted in fatalities (Appel et al., 1975). Iodomethane has been a fairly common alkylating agent in undergraduate organic chemistry courses. Bromomethane is more widely preferred in commercial processes because it is much less expensive. The potential population and environmental target for contact with iodomethane is relatively limited, although identifiable.

5. From Disposal

As industrial chemicals go, monohalomethanes range from moderately expensive (bromo and chloromethane) to very expensive (fluoro and iodomethane). There is therefore economic pressure on commercial users to conserve and recapture these chemicals when feasible, and not to simply vent excess materials to the environment, although the possibility of that occurring exists.

Fluoromethane and iodomethane are used in such small quantities that environmental contamination via disposal of these chemicals is not likely to be significant.

More than 90% of the chloromethane produced in this country is used to make other chemicals, so only a small fraction of the total production could possibly be released to the environment from disposal.

Much of the bromomethane manufactured is released to the environment during its major use as a fumigant. Additional release, if any, from disposal practices is likely to be insignificant by comparison.

6. Potential Inadvertent Production in Industrial Processes

There are a number of industrial and related chemical processes in which a monohalomethane has been reported to be a side product. This is not surprising in view of the simplicity of these molecules and the ubiquity of the chemical species from which they can be formed.

Chloromethane has been identified as a minor product in the incineration of garbage (Busso, 1971). It was one of the many organics said to total up to 1.5 kilograms per ton of garbage incinerated per hour at nine different municipal waste incinerator plants in France.

The presence of chloromethane in drinking water (see Table 20) suggests its possible formation during the process of chlorination. Stevens et al. (1976) studied conditions favoring the formation of chloroform during the chlorination of drinking water; the same conditions may also favor the formation of monohalomethanes as borne out by the data presented in the monitoring section of this review.

Dennis et al. (1972) detected chloromethane formed as a result of the use of bromomethane as a fumigant on stored wheat. The amount of chloromethane detected varied with the type of stored product. None was found with fumigated peanuts, soybeans, and peas; but it was detected with wheat, flour, corn, cornmeal, and wheat germ.

Bromomethane is a side product in the reaction to produce tribromosalicylanilide, a minor synthetic reaction. Bromomethane is generated in sufficiently high concentrations to have been responsible for two reported cases of bromomethane poisoning, one of which resulted in permanent brain damage to a 62 year old chemist (Araki et al., 1971). It is obvious that whenever a chemical process has the potential for forming a monohalomethane, precautions should be taken to avoid similar incidents.

The industrial activity likely to give rise to the most serious potential environmental hazard involving a monohalomethane is the production of energy via nuclear fission reactors. Iodine is one of the more volatile core fission products that can be evolved during normal operation of the reactor (Thompson and Kelley, 1975). In the event of a major accident such as a broken main coolant pipe, the ensuing release of airborne fission products to the containment building and the outside atmosphere is something that power companies must postulate will occur, then develop strategies to avoid (Parsly, 1971). The isotope of most concern is ^{131}I which has a half life of 8.04 days. ^{129}I, with a half life of 1.59×10^7 years, is of less concern because of its low specific activity (Thompson and Kelley, 1975). Iodine may be present in nuclear reactors as inorganic iodide, elemental iodine, or organic iodine. The form which has received the most attention is iodomethane, first because of its abundance as a fission product, and second because it is volatile, relatively insoluble in water, difficult to coagulate or adsorb on reactor walls or containment surfaces, and can contaminate mankind in the food chain of air, grass, cow, and milk (Heinemann et al., 1974). The formation of iodomethane in nuclear reactors is essentially independent of the temperature because iodination reactions are very effectively induced by the presence of radiation (Barnes et al., 1967). Therefore, even in the event of a shutdown in the heat exchange system of a reactor, the rate of formation of iodomethane and the hazard therefrom may be significant.

Various control technologies have been developed to routinely remove iodomethane from core reactor air in nuclear power plants as well as from air contained within a plant which has sustained a major accident. These techniques are summarized in Table 15. The two general approaches taken are either to cause the iodomethane to react to form compounds which are nonvolatile and easily coagulated or dissolved in water (e.g., reduction to iodide with

Table 15. Methods of Iodomethane Control in Nulear Fission Reactors

Method	Reference
Aerosol formation with hydrazine	Viles and Silverman, 1966
Reactive foams	Viles *et al.*, 1968
Activated charcoal	Ludwick, 1969 Bennett and Strege, 1972; 1974; 1975 Bellamy, 1974 May and Polson, 1974
Continuous sprays	Postma and Coleman, 1970 Owzarski *et al.*, 1974
Nitric acid scrub (Iodex Process)	Groenier, 1973
Chlorine exchange	Slagle, 1973
Silver zeolites	Thompson and Kelley, 1975

hydrazine (Viles and Silverman, 1966) or reaction with thiosulfate (Owzarski et al., 1974), or absorption on special filtering media (e.g., activated charcoal (see Table 15) or zeolites (Thompson and Kelley, 1975)).

7. Natural and Inadvertent Production in the Environment

Considerable evidence is available to suggest that most of the chloromethane, bromomethane, and iodomethane detected in the environment can be attributed to natural sources (Lovelock, 1975; Grimsrud and Rasmussen, 1975; Singh et al., 1977). Lovelock et al. (1973) suggested that the annual production of iodomethane would have to be 80 x 10^9 lbs. (40 megatons) based upon environmental monitoring and stability considerations. The commercial production of 20,000 lbs. in the U.S. is obviously an insignificant contamination source. Sizable quantities of iodomethane are converted to chloromethane in seawater before the iodomethane evaporates (Zafiriou, 1975). Lovelock (1975) has suggested a chloromethane source strength of 56 x 10^9 lbs. per year which is considerably more than 0.423 x 10^6 lbs. per year which is annually manufactured in the U.S. Wofsy et al. (1975) have indicated that 75 to 95% of the bromomethane contamination in the environment can be attributed to natural sources.

Other sources of monohalomethanes have been suggested. Chloromethane has been identified as a breakdown product of an analog of the insecticide DDE, which itself is a photolysis product and metabolite of DDT (Silk and Unger, 1972). Chloromethane has also been found in tobacco smoke, where it was attributed to the thermolysis of p,p'-DDT as its concentration in the smoke was proportional to the concentration of the insecticide in the tobacco (Chopra and Sherman, 1972). Fumigation of certain foods with bromomethane can give rise to formation of chloromethane (Dennis et al., 1972). The amount of chloromethane which forms depends on the particular food involved. The formation of chloromethane may therefore be related to the chlorine content of the food. The photolysis of gaseous chloroethane (a solvent) gives rise to chloromethane as one of the products (Cremieux and Herman, 1974), which suggests that monohalomethanes may be formed by photolytic decomposition of higher alkyl halides in the environment.

It has been suggested that a possible source of bromomethane may be the decomposition of dibromomethane, a common gasoline constituent, during gasoline combustion (Wofsy et al., 1975). The accuracy of the suggestion is unknown since ethylene dibromide is the only bromine compound that is added to gasoline in significant quantities.

No specific data was found for inadvertent production in the environment of fluoromethane.

D. Analytical Methods

1. General Methods for Halocarbons

This section describes methods which are suitable for more than one halocarbon. The succeeding sections are devoted to methods developed exclusively for a particular halomethane (but which usually are applicable to others as well).

Classical sodium fusion schemes for determining halogens in organic compounds involve destroying the organic moiety and converting the halogen into the ionic halide which can then be titrated via the Mohr, Volhard, or other usual wet methods. A sodium fusion variation has been reported by Menville and Parker (1959). It allows an entire determination in one step which takes about fifteen minutes. This method is useful for monitoring the purity of standard samples of monohalomethanes, especially iodomethane.

A method for the microdetermination of chlorine, bromine, and iodine in organic compounds has been described by Cook (1961). The sample containing an equivalent of 0.1 mM halogen is burned in oxygen in the presence of a small quantity of reagent grade sodium nitrate; the contents of the combustion flask are then titrated with standardized mercuric nitrate. The method does not distinguish inorganic from organic halogens, and like the previous method it is also most useful for solid or liquid compounds of relatively high purity.

The problem of analyzing gas samples for monohalomethanes has been examined mainly from the point of view of fumigant detection and control as well as to detect trace quantities of halomethanes from natural and manmade sources. One approach is to catalytically oxidize the sample, convert halogens to the elemental state, then detect them in the galvanic cell of a gas analyzer (Waclawik and Waszak, 1970). For chlorinated hydrocarbons a range of 0 - 3 ppm (as Cl_2) with a minimum accuracy of 0.3 ppm is claimed for the method. Sidor (1969) adapted a similar scheme for field use. The oxidation products are drawn through a solution of phenol red, halogenation of which is detected by specific absorption peaks for the chloro-, bromo-, and iodo- derivatives. The technique is sufficiently sensitive to detect halogenated compounds in air at concentrations of 1.0, 0.1, and 0.5 ppm, respectively, for compounds of chlorine, bromine, and iodine in 10 ℓ air samples taken at the rate of 1 ℓ/min using 10 ml of absorbing solution in the air impinger. Sampling efficiency is close to theoretical. The method is suitable for long term monitoring as well as spot checks. It has been used to determine bromomethane and iodomethane in the field.

Murray and Riley (1973) have used gas chromatography to determine chlorinated aliphatic hydrocarbons in air, natural waters, marine organisms, and sediments. Air samples are passed through activated charcoal traps from which the chloroalkanes are stripped by heating in a stream of nitrogen. Water samples are stripped by bubbling nitrogen through them. Sediments and tissues of marine organisms are stripped by heating them in a current of nitrogen. The haloalkanes in the nitrogen stream are collected on a column packed with a silicone coated stationary phase cooled to -78°C. When stripping is complete, the column is gradually warmed and the chloroalkanes swept by argon into a gas chromatograph with equipped with an electron capture detector. In addition to detecting chloromethane at concentrations less than 1 ppm, this study detected chloroform, carbon tetrachloride, trichloroethylene, and other common industrial solvents. The results are further discussed in the section on monitoring (II-E, p. 80).

Gas phase coulometry has been used to detect a variety of halocarbons in air, including iodomethane (Lillian and Singh, 1974). The method is extremely sensitive, easily allowing measurements in the ppb range. The halocarbons are separated in a gas chromatograph and detected with two electron capture detectors in series. The high sensitivity is due to the absolute nature of the detectors at 100% ionization efficiency; in effect, the system responds to every molecule of sample, avoiding mixing and contamination errors inherent in dilute calibration mixtures. At ionization efficiencies of less than 100%, the use of two detectors in series enables determination of the fractional ionizations and thereby maintains the absolute nature of analysis by correcting for unionized molecules. The results of this study of air in New Brunswick, New Jersey, are discussed in the section on monitoring (II-E).

A mass spectrometry/gas chromatography system developed by Grimsrud and Rasmussen (1975) is sensitive to monochlorinated hydrocarbons in the parts per trillion range with a precision of ±5%. A typical analysis of chloromethane is shown in Fig. 8. Findings of chlorinated hydrocarbons in the atmosphere of the rural northwest are discussed in section II-E.

While gas chromatography is well established as a method of choice for separating and detecting halocarbons in natural waters, there are a variety of extraction procedures to choose from. Gas stripping has already been described above (Murray and Riley, 1973). Another approach is to equilibrate the dissolved hydrocarbon with a small volume of gaseous headspace under reduced pressure and elevated temperature, then inject headspace samples into a gas chromatograph (Kaiser and Oliver, 1976). Quantitative determination in the range 0.1 - 10 ppb is possible with small samples (∿60 ml). This method has

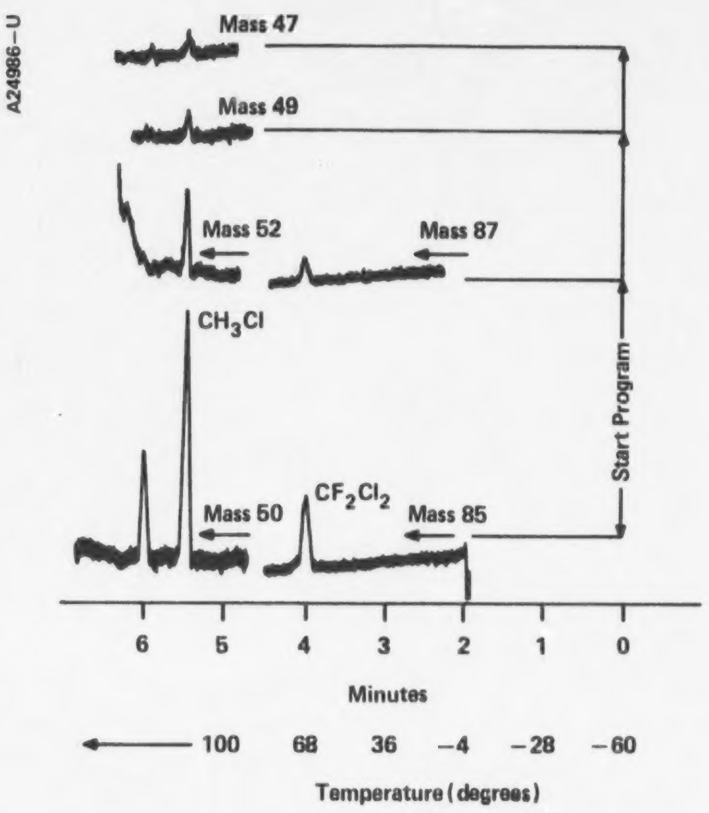

Figure 8. Typical analysis of chloromethane and dichlorodifluoromethane in a 20 cm^3 sample of rural southeastern Washington air. The gas chromatographic effluent is monitored by a mass spectrometer operating in the single ion mode. (Grimsrud and Rasmussen, 1975)

been used with chloroform and various chlorobromomethanes, but not monohalomethanes. Another technique for extracting and concentrating halomethanes from water samples involves shaking the sample with pentane followed by analysis of the pentane extract via gas chromatography (Richard and Junk, 1977). Quite small samples (~10 ml) in the concentration range 0.1 ppb were successfully extracted. Here also, the compounds studied were halomethanes, but not monohalomethanes, although the technique should be equally applicable to all halomethanes.

2. Fluoromethane

None of the literature examined dealt specifically with either the monitoring or determination of fluoromethane. However, the gas chromatography and mass spectrometry methods described for other halomethanes might be adaptable for fluoromethane.

3. Chloromethane

Redford-Ellis and Kench (1960) reported a spectrophotometric method for chloromethane. It is, however, of historical interest only, having the major disadvantages of being nonspecific and tedious. A much better method for chloromethane is that of Grimsrud and Rasmussen (1975), described above.

4. Bromomethane

More analytical attention has been focused on bromomethane than all of the other monohalomethanes combined, chiefly because of its role as a fumigant and the resulting need to determine residues of bromomethane on foodstuffs, in soils, and air.

Bromomethane assays provide up to four kinds of information: total bromides, inorganic bromides, bromomethane in air, and bromomethane residues (other than in air). It is necessary to distinguish between assays for bromine and/or bromide residues and those for bromomethane or other organic bromine. Often it is the total bromine, regardless of origin, which is determined (Getzendaner, 1975). Total bromide is valid where naturally occurring background bromide is sufficiently low to be neglected (which is often not the case) or else is known and can be taken into account. On occasion the investigator is only interested in inorganic bromides resulting from fumigation. (Bromomethane decomposes rapidly after fumigation and within a few days is completely in the form of inorganic bromide.) The determination of bromomethane in air is an important aspect of fumigation safety practices. Several techniques for bromomethane in air have been previously discussed. Finally, the determination of bromomethane in fumigated commodities is often necessary as a means of ascertaining the thoroughness and uniformity of the fumigation technique. A pile of wheat can behave as a chromatographic column for bromomethane (Berck and Solomon, 1962), which suggests that fumigation and sampling techniques must be adjusted to avoid the potential problems arising from this phenomenon.

All four of these approaches to assaying bromomethane have been reviewed in detail by Malone (1971) and more recently (for foods and feeds) by Getzendaner (1975). We shall highlight these extensive reviews here, with emphasis placed on recent material not included in the reviews.

a) Total Bromides

The general approach to total bromides is to hydrolyze the sample with alcoholic potassium hydroxide, then oxidize the resulting bromide ion to bromate with acidified sodium hypochlorite;

$$3OCl^- + Br^- \xrightarrow{H^+} BrO_3^- + 3Cl^-$$

The excess hypochlorite is reduced with sodium formate:

$$HOCl + HCOO^- \rightarrow Cl^- + CO_2 + H_2O$$

The bromate is reacted with potassium iodide, liberating free iodine which is titrated with standardized thiosulfate:

$$BrO_3^- + 6KI + 6H^+ \rightarrow 6K^+ + Br^- + 3I_2 + 3H_2O$$

$$2S_2O_3^= + I_2 \rightarrow S_4O_6^= + 2I^-$$

The sensitivity of the procedure is due to the reaction of six thiosulfate ions for every bromate ion. This technique has been applied to total bromide analysis in many studies of bromide accumulation in plants grown in soil fumigated with bromomethane, an example of which is the study of lettuce plants by Kempton and Maw (1972).

b) Inorganic Bromides

Inorganic bromides are the chief residue of fumigations with bromomethane. The volatility of the parent compound causes it to dissipate quickly in most cases. Sometimes it is assumed that the only bromine present is as bromide, and the samples are treated the same as for total bromides after the hydrolysis step.

Inorganic bromides can be removed from samples by extraction with aqueous methanol, although a better procedure is to first extract all organic bromine compounds with chloroform, then assume any bromine compounds remaining are inorganic. Heuser and Scudamore (1970) described a different approach in which inorganic bromide was determined in the presence of organic bromide by reacting the inorganic bromide with ethylene oxide to form ethylene bromohydrin, which was then extracted with diisopropyl ether and acetonitrile, leaving the organic bromine (bromomethane and bromoethene) intact. All three compounds were determined by gas-liquid chromatography. Not only was the inorganic bromine distinguished from the organic bromine, but the two sources of organic bromine were distinguished from each other.

c) Bromomethane in Air

Techniques for bromomethane in air were previously discussed above, under general methods for halocarbons. Gas chromatography is the method of choice when quantitative results are desired and/or trace quantities of bromomethane are to be determined.

Mixtures of bromomethane and dibromoethene in air with other fumigant ingredients may be separated and detected by differential hydrolysis followed by amperometric titration (Berck, 1961). Muthu et al. (1971) reported a bioassay for bromomethane and a number of other fumigants which is useful for the high concentrations likely to be encountered in an enclosed fumigated area (on the order of 10,000 ppm). The method depends on observing the effect of an air sample on insects. The results agreed within 10% with chemical assays on the same air samples.

Certain qualitative techniques for bromomethane in air are also available, such as commercial halide leak detectors which operate by burning acetylene or anhydrous methanol, both of which give nearly colorless flames when pure. The presence of bromomethane imparts a green to blue color to the flame, the exact hue and intensity of which is proportional to the concentration of the bromomethane. These detectors operate over a range of approximately 40 - 800 ppm (Kereluk, 1971).

A gas dilution system for obtaining standard air-diluted samples of bromomethane has been developed by Scheide et al. (1973) for NIOSH. Concentrations between 5 - 100 ppm can be produced accurately and reproducibly with this system. Bromomethane is sufficiently stable in steel storage containers so that the concentration of the calibrated mixtures varies less than 1% in 30 days (at 1000 ppm).

d) Bromomethane Residues

When it is necessary to determine bromomethane residues (without inorganic bromides) on fumigated commodities, the fumigant may be separated from the sample by aeration or a suitable solvent. Heuser and Scudamore (1968) have used a 5:1 mixture of acetone and water to extract bromomethane and ethylene oxide from wheat and flour. An extraction efficiency better than 95% was achieved. Gas chromatography was used to detect the fumigant constituents. The sensitivity limit for bromomethane was 0.3 ppm. A more extensive scheme involved gas-liquid chromatography with electron capture detectors optimized for a total of twenty fumigant residues on foodstuffs, which achieved a lower limit of sensitivity for bromomethane of 0.1 ppm (Heuser and Scudamore, 1969; 1970).

Multiple residues of fumigants in grains have been extracted by acid reflux and detected via electron capture gas chromatography (Malone, 1970). X-ray fluorescence spectroscopy has been used to determine bromine in wheat damaged by excess bromomethane in the soil (Brown and Jenkinson, 1971). This method claims an accuracy of approximately 2 - 3% or 2 ppm, whichever is larger; the lower limit of sensitivity for bromomethane is 0.3 ppm in wheat, 0.7 ppm in soil.

5. Iodomethane

McFee and Bechtold (1971) reported a very effective analytical system for iodomethane, consisting of a pyrolyzer and microcoulomb detector which offers a lower limit of sensitivity of 2 ppb. Although the detector is insensitive to many solvent hydrocarbons, it is nondiscriminatory towards halocarbons and those of low molecular weight are especially likely to interfere with the detection of iodomethane. However, it has the virtue of providing a continuous signal and could therefore serve as a monitoring method in environments where iodomethane is known to be the main potential hazard.

A colorimetric method for iodomethane has been reported by Rangaswamy et al. (1972). It depends on the ability of iodide ion to catalyze the reduction of ceric ions by arsenous ions. Iodomethane is hydrolyzed by KOH to produce iodide, the concentration of which determines the rate of the redox reaction; after a specific time period has elapsed the absorption of the remaining Ce(IV) is therefore proportional to the concentration of the iodomethane in the original sample. The method requires at least 0.01 μg/ml iodide in solution (ca. 3 ppm), but the actual sensitivity depends on the composition of the original sample and the extraction procedure.

Radioactive isotopes of iodine (e.g., ^{129}I, ^{131}I) represent one of the more significant biological hazards of nuclear fission reactors. Elemental iodine and iodomethane are the major forms in which radioactive iodine is produced in reactors. Iodomethane is the most elusive of iodine species identified in fission product release; it is difficult to trap. Iodine-impregnated charcoal effectively absorbs iodomethane (Bennett et al., 1968), although it is not an ideal sampler at the high temperatures encountered in reactor cores. Silver-zeolite filters are also very effective (Thompson and Kelley, 1975) as well as expensive. Wilhelm and Scheuttelkopf (1973) have suggested the use of an amorphous silicic acid catalyst carrier material impregnated with silver nitrate as a compromise for efficient trapping of iodomethane at high temperatures and relative humidities. The silicic acid impregnated with silver nitrate is about three times the cost of iodine-impregnated charcoal, but much less than silver-zeolite.

Iodomethane can be detected in the presence of methanol and nitromethane via a gas chromatography technique developed by Apple et al., (197[illegible]) to study unreacted iodomethane from fission reactor gas streams scavenged by 20 M nitric acid (the CH_3I is not removed by the nitric acid). Twenty-two μg of iodomethane were detected in a typical 5 μℓ sample; the sensitivity of the system was not given, but appears to be much better than this example suggests.

Stanford Research Institute, under contract to NIOSH, developed an analytical method for iodomethane in air which has been validated for the 3 - 9 ppm range (U.S. Department of Commerce, 1975). The sampling device is small and portable; results are obtained quickly. The principle of the method is to extract the iodomethane by passing the air through a charcoal filter which is later eluted with toluene. Aliquots of the toluene eluent are injected into a gas chromatograph where the retention time and peak area of the sample are compared to standards. Excessive humidity at the sampling site interferes with the collection of iodomethane. Also, other substances with the same retention time for a given gas chromatographic system will interfere.

Table 16 presents a summary of the analytical methods for halomethanes.

Table 16. Selected Analytical Methods for Monohalomethanes

Technique	Method Tested with or Suitable for	Sensitivity	Reference
Colorimetry	CH_3Cl, CH_3Br, CH_3I	1.0, 0.1, 0.5 ppm, respectively	Sidor, 1969
Colorimetry	CH_3I	~3 ppm	Rangaswamy *et al.*, 1972
Colorimetry, Flame	CH_3Br	40 ppm	Kereluk, 1971
Coulometry	CH_3Cl	<1 ppm	Waclawik and Waszak, 1970
Coulometry	CH_3I	2 ppb	McFee and Bechtold, 1971
Coulometry, Gas Phase	CH_3I	ppb range	Lillian and Singh, 1974
Gas Chromatography	Halomethanes	0.1 - 10 ppb	Kaiser and Oliver, 1976
Gas Chromatography	Halomethanes	0.1 ppb	Richard and Junk, 1977
Gas Chromatography	CH_3I	<3 ppm	U.S. Dept. of Commerce, 1975
Gas Chromatography (electron capture)	CH_3Cl	<1 ppm	Murray and Riley, 1973
Gas-Liquid Chromatography (electron capture)	CH_3Br	0.1 ppm	Heuser and Scudamore, 1969, 1970
Gas Chromatography/Mass Spectrometry	CH_3Cl	5 ppt	Grimsrud and Rasmussen, 1975
X-Ray Fluorescence	CH_3Br (wheat residues)	0.3 ppm	Brown and Jenkinson, 1971

E. Monitoring

Monohalomethanes have been detected in the atmosphere, in water, including drinking water, in fumigated soils, and in human food and animal feedstocks. Fluoromethane, alone among the four compounds, has not been reported in monitoring studies. Chloromethane, bromomethane, and iodomethane have all been found in air and water. Bromomethane has been detected in fumigated soils and also in food products fumigated at some point during processing. In addition, bromide residues have been detected in food products grown in bromomethane-fumigated soil or exposed to bromomethane fumigants during storage or processing. In this section, each of the four major areas of monitoring will be considered separately.

1. The Atmosphere

In 1973 Lovelock et al. reported several halogenated hydrocarbons in the air over the Atlantic Ocean, including iodomethane. Considerable local variation in the concentration of iodomethane suggested marine algae as the origin of this compound. It is estimated that marine algae produce about 40 million tons of iodomethane annually (Lovelock et al., 1973), which means it may be a key compound in the natural cycle of iodine between land and sea. In spite of the large quantity produced, iodomethane has a mean residence time in air of only 50 hours, which results in a low mean concentration in the air of 1.2×10^{-10} by volume. The sole destructive process appears to be photolysis by sunlight.

Iodomethane has been detected in the air over New Brunswick, New Jersey, at a concentration of 0.08 ppb (Lillian and Singh, 1974). This concentration is approximately two-thirds to one-quarter the value of other halocarbons monitored at the same time (see Table 17).

Table 17. Ambient Concentrations of Coulometrically Determined Compounds in the New Brunswick, N.J., Area*

Compound	Concentration, ppb
CCl_3F	0.37
CH_3I	0.08
CH_3CCl_3	0.27[a]
CCl_4	0.17
$CHCl = CCl_2$	. . .[b]
$CCl_2 = CCl_2$	0.12

[a] Based on an ionization efficiency of 20%.

[b] Not amenable to anaylsis (Ionization efficiency = 0).

* Lillian and Singh, 1974

Grimsrud and Rasmussen (1975) surveyed the atmosphere over the rural southeastern areas of the state of Washington and detected 19 simple halocarbons including chloromethane (530±30 ppt), bromomethane (< 5 ppt), and iodomethane (< 5 ppt). By way of comparison to these concentrations, other halocarbons found were carbon tetrachloride (120±30 ppt), chloroform (20±10 ppt), and dichlorodifluoromethane (230±10 ppt), among other compounds. The concentration of chloromethane was found to be relatively constant throughout ∿2½ miles of the lower troposphere over the city of Pullman, Washington (Table 18). Since industrial production cannot account for either the uniformity of distribution nor the total quantity of chloromethane, the oceans are proposed as the major likely source of chloromethane in the atmosphere. Biota in the oceans could release chloromethane; it is known to be a product of certain living processes, for example, some types of microbial fermentation (Lovelock, 1975). Another possible source of chloromethane in the oceans is indirect emission as a result of the reaction of chloride ions with iodomethane; the high concentration of chloride ions in the ocean could result in nucleophilic displacement of iodine from iodomethane.

Chloromethane has also been detected in the air over the coastal waters of southern England (Lovelock, 1975) in amounts which are taken as confirming chloromethane as the dominant halocarbon of the atmosphere. Trichlorofluoromethane was also monitored in this study (see Fig. 9).

Two field studies in California (Singh et al., 1977) identified chloromethane, bromomethane, and iodomethane in the atmosphere, as well as the Freons 11, 12, 113, and other halocarbons (see Table 19). The sampling sites were Point Reyes, about 30 miles south of San Francisco, and Stanford Hills,

Table 18. Methyl Chloride and Dichlorodifluoromethane Concentrations Above and In the City of Pullman*, Washington, 12 December 1974.

Sampling site	CH_3Cl
12000 ft	558
10000 ft	503
8000 ft	564
6000 ft	550
4000 ft	566
WSU campus	503
Downtown Pullman	518

*Pullman elevation 2550 ft. in SE corner of Washington State, prevailing winds from SW.

(Grimsrud and Rasmussen, 1975)

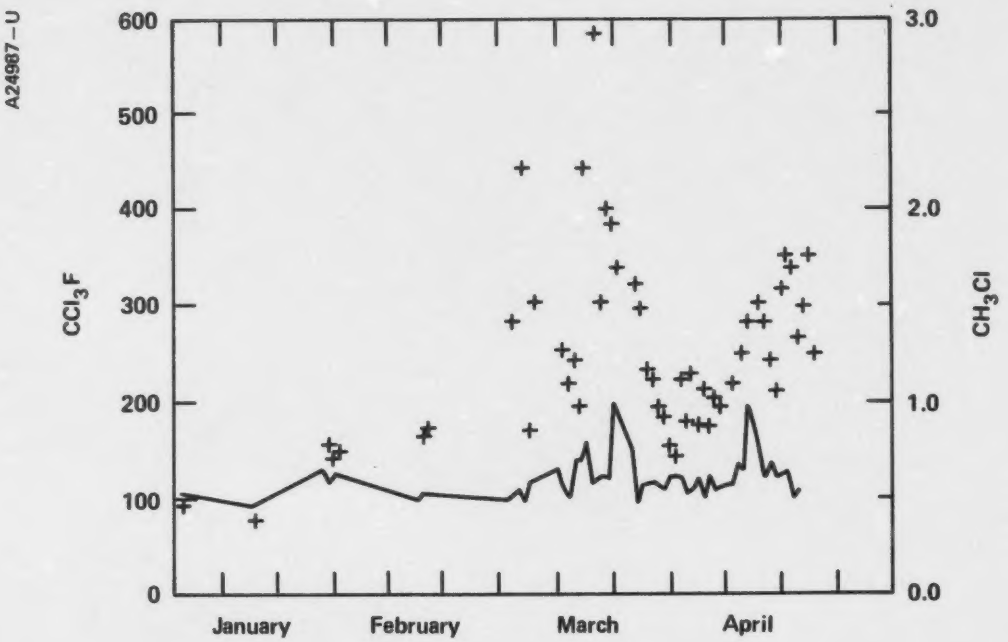

Figure 9. Aerial concentration of CH_3Cl (+) and of CCl_3F (solid line) in parts per 10^9 and 10^{12} by volume respectively. (Lovelock, 1975)

Table 19. Summary of Halocarbon, SF_6, and N_2O Monitoring Data*

			Site 1			Site 2				
			Monitoring period 11/24/75–11/30/75			Monitoring period 12/02/75–12/12/75				
Compounds	Major source assignment	Lower detection limit (ppt)	No. of data points	Measurement frequency[b] (percent)	Average background concentration (ppt)	No. of data points	Measurement frequency[b] (percent)	Average background concentration (ppt)	Average background concentration (ppt) of Sites 1 & 2	Shorewater concentration[e] (ppt) at Site 2
N_2O	N	1000	132	100	291.0×10^3 $(6.7 \times 10^3)^c$	147	100	300.9×10^3 (7.4×10^3)	296.0×10^3	
SF_6	A	0.02	41	100[d]		83	100	0.16 (0.02)	0.16	
F12	A	5	63	100	182.0 (6.3)	126	100	179.6 (12.2)	180.8	36
F11	A	1	166	100	104.0 (5.5)	360	100	103.3 (6.6)	103.8	43
F113	A	2	72	100	15.7 (3.3)	202	100	16.9 (3.3)	16.3	23
CCl_4[a]	A	1	246	100	113.9 (3.8)	564	100	114.5 (11.6)	114.2	85
CH_3Cl	N	200	65	100	780.6 (110.5)	127	100	1011.4 (209.2)	952.9	1200
$CHCl_3$	A	2	187	100	20.5 (3.7)	450	100	26.2 (5.9)	23.4	2854
CH_3I	N	1	69	100	1.9 (0.6)	204	100	2.9 (0.8)	2.4	37
CH_3CCl_3	A	2	75	100	77.6 (6.2)	300	100	90.3 (10.6)	84.0	140
CCl_2CCl_2	A	5	118	100	38.3 (11.1)	257	100	43.1 (17.8)	40.7	149
$CHClCCl_2$	A	6	115	95	14.6 (5.0)	255	48	14.1 (4.0)	14.4	153
CH_3Br	N	30	64	8	30 (0.0)	117	16	52.8 (16.5)		140

N = Natural, A = Anthropogenic

[a] Small natural sources may also exist.

[b] Defined at concentrations above the lower limit of detectability.

[c] Quantity in parenthesis is the standard deviation.

[d] At Site 1 cryogenic concentrations were not operative, and while SF_6 was observable by direct injections no quantification was possible at concentrations below 0.5 ppt.

[e] This concentration is defined as the concentration of the constituent in helium in equilibrium with the water.

*Singh et al., 1977

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California, about 30 miles north of San Francisco. The chloromethane concentrations approached nearly an order of magnitude greater than the individual concentrations of the Freons. The overall concentration of chloromethane was found to be 952.9 ppt. While low anthropogenic sources support the concept of the ocean as the dominant source for the quantities of chloromethane monitored, Singh et al. (1977) believe that marine sources cannot account for the entire amount of chloromethane detected.

Besides chloromethane, Singh et al. (1977) identified iodomethane in the air over the Pacific Ocean at an average concentration of 2.4 ppt, with an estimated half life of less than two days. The abundance of iodomethane in the oceans (see below) is cited by Singh et al. (1977) as well as by Lovelock (1973) as evidence that the sea is the major natural source of iodomethane.

Bromomethane could not be detected in all samples taken from the two sites monitored by Singh et al. (1977). The average level of bromomethane found at the Stanford Hills site was 16-18 ppt.

Chloromethane was monitored over Kenya in southern Africa (Lovelock as reported in Block et al., 1977) at a concentration of 2.9×10^{-9} (v/v). The ocean and smouldering vegetation were identified as sources. Air pollution monitoring in the Soviet Union has resulted in the detection of chloromethane in the atmosphere near a synthetic rubber plant (Aliverdieva and Minchuk, 1973). It is likely the source of the detected chloromethane is anthropogenic since chloromethane is a solvent for the polymerization of isoprene.

2. Water

All of the halomethanes, with the exception of fluoromethane, have been monitored in a variety of waters, including drinking water, chemical plant effluents, river water, sewage treatment plant effluent, and the oceans. Shackelford and Keith (1976) compiled a list of all fresh water monitoring data known to the Environmental Protection Agency through mid-1976. Data from this source is summarized in Table 20 for each monohalomethane. Where the information was available, monitoring sites, dates, and specific references are included in the table.

Iodomethane has been found in all marine waters monitored by Lovelock (1975) at a mean surface water concentration of 135 x 10^{-12} ml(of vapor)/ml water. Iodomethane is believed to be distributed throughout the oceans (Lovelock _et al._, 1973), with marine algae the main source. Although local variations in concentration were noted by Lovelock, there was no obvious change in concentration with latitude. Data for iodomethane in the Atlantic, Caribbean, and Antarctic Oceans are given in Table 21. Data for chloromethane, bromomethane, and iodomethane in water sampled from the seashore at Kimmeridge, Dorset, England, is presented in Table 22. The waters of the Kimmeridge site are rich in kelp, thought to be the main source of these halomethanes at this site. The much greater concentrations of halomethanes in sea water as compared to the surrounding air (see Table 23) are taken as evidence that the oceans are the origin of naturally produced halomethanes.

Kleopfer (1976) reported dibromochloromethane, bromodichloromethane, and bromoform in the tap water of Evansville, Indiana. Monohalomethanes were not reported. Other halomethanes were found in the tap water of Jefferson City, Missouri; Kirkwood, Missouri; Kansas City, Kansas; and Johnson City, Kansas.

Table 20. Monohalomethanes Identified in Water[a]

CHLOROMETHANE

1. Effluent from a chemical plant (10/75)[b], Calvert City, Kentucky
2. River water (11/73), Chromatographia, 7, 118 (1974)
3. Effluent from sewage treatment plant, Emile Coleman, EPA, Cincinnati, Ohio
4. Finished drinking water, Dordrecht, Germany
5. Finished drinking water (1970), EPA Report, Region VI, Dallas, Texas, April 1972
6. Finished drinking water (1/76), Bob Tardiff, EPA, Cincinnati, Ohio
7. Finished drinking water, Durham, North Carolina, "Identification and Analysis of Organic Pollutants in Water," L.H. Keith, Ed., Ann Arbor Science Publishers, June 1976
8. Effluent from a chemical plant (8/75), Louisville, Kentucky
9. Finished drinking water (4/75), Miami, Florida
10. Finished drinking water (1/75), Cincinnati, Ohio, EPA Report to Congress, December 1975, "Preliminary Assessment of Suspected Carcinogens in Drinking Water"
11. Finished drinking water (1/75), Iowa, ibid.
12. Finished drinking water (1/75), Philadelphia, Pennsylvania, ibid.
13. Effluent from a chemical plant (8/73), Pacolet and Noree River, South Carolina
14. Rhine River
15. River water (7/75), G.A. Junk and S.E. Stanley, Ames Laboratory, ERDA, Iowa State University, Ames, Iowa

BROMOMETHANE

1. Finished drinking water (1/76), Bob Tardiff, EPA, Cincinnati, Ohio
2. Finished drinking water, Miami, Florida, EPA Report to Congress, December 1975, "Preliminary Assessment of Suspected Carcinogens in Drinking Water"
3. Finished drinking water (7/75), G.A. Junk and S.E. Stanley, Ames Laboratory, ERDA, Iowa State University, Ames, Iowa

IODOMETHANE

1. Finished drinking water (1/76), Bob Tardiff, EPA, Cincinnati, Ohio

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[a] Shackelford and Keith, 1976.
[b] Monitoring dates, where available, are indicated by parentheses.

Table 21. Iodomethane in Surface Seawater[a]

Date	Site	Concentration[b]
1971-72	Open ocean Atlantic and Antarctic	135 (248)
1973	Open ocean Atlantic and Caribbean	138 (47)
1973	SW Ireland	3.4 (1.8) x 10^3
1973	Kelp beds SW Ireland	1.2 (0.9) x 10^5

[a] Lovelock, 1975

[b] Concentrations as ml of vapour per ml of water x 10^{-12}. Figures in parentheses are standard deviations.

Table 22. Halomethanes[a] in Water From the Seashore at Kimmeridge, Dorset, England[d]

Date	Water Temperature (°C)	CH_3Cl	CH_3Br[b]	CH_3I
12/1/75	45	7.2 (2.7)[c]	2.0 (0.7)	1.3 (0.3)
8/3/75	42	5.9 (0.8)	1.5 (0.30)	1.2 (0.3)
9/4/75	42	21 (12)	3.9 (2.0)	2.8 (0.7)

[a] Concentrations are in ml of gas per ml of water x 10^{-9}.

[b] CH_3Br confirmed by retention time only.

[c] Figures in parentheses are standard deviations.

[d] Lovelock, 1975

Table 23. Detected Levels of Halogenated Hydrocarbons[a]

	CCl_3F	CH_3I	CCl_4
Mean aerial concentration x 10^{-12}	49.6 (7.1) [b]	1.2 (10.0)	71.2 (6.86)
Mean surface water concentration ml. of vapor $ml.^{-1}$ water	7.6 (7.2)	135 (248)	60 (17)
Annual production rate (megatons)	0.44	40	1.7
Residence time (yr)	>10?	0.003	1

[a] Lovelock *et al.*, 1973

[b] Figures in parentheses are standard deviations.

Traces of chloromethane and iodomethane were found in Miami, Florida, drinking water using a fractional purging-gas chromatography/mass spectrometry technique developed by Kopfler _et al_. (1976) during the National Organics Survey (NORS) of drinking water.

Bromomethane has been identified in the drinking water of six communities in central Iowa (Richard and Junk, 1977) via an extraction-electron capture gas chromatographic procedure sensitive to 0.1 μg/ℓ in a 10 ml sample. The concentration of the bromomethane monitored at six sites ranged from 0.1 - 0.4 μg/ℓ. Also identified in concentrations at least ten times greater than bromomethane, were chloroform, dibromochloromethane, and bromodichloromethane.

3. Soil

Kolbezen _et al_. (1974) studied factors that affect the deep penetration of bromomethane into field soils by monitoring soils for up to forty days after fumigation with bromomethane. A variety of soil types (i.e., sandy, silty, clay) were chosen. The effect of such parameters as moisture was examined. Some of the data obtained is shown in Table 24. The diffusion of bromomethane in soil was found to be generally downward in a cone shaped pattern. Injection of the fumigant at three to five foot depths resulted in penetration up to 9 - 12 feet from the surface, depending on soil characteristics. Concentrations near the surface of the soil were very low to zero because of the rapid escape of bromomethane near the surface into the atmosphere. Drier and more porous soils showed greater penetration and broader diffusion patterns than moist, dense soils. Diffusion in wet (especially saturated) soils is extremely slow because of the very low solubility of bromomethane in water. The monitoring data obtained in this study were used to develop fumigation practices for

Table 24. Concentration of Bromomethane in Soil Atmospheres of Moreno Silt Loam Soil at Various Depths and Distances at Various Times After Application[a]

MB (ppm) applied June 2, 1969†				
Depth and P_w*	Days after applic.	Lateral distance from application point (ft.): 2	5	8
1 ft /19%	1			
	2			
	3			
	7			
	10			
	15			
	25			
3 ft /27%	1			
	2			
	3	15		
	7	119		
	10	251		
	15	327		
	25	12		
6 ft./23%	1	56		
	2	1,590		
	3	8,350	32	
	7	3,790	250	
	10	2,790	400	15
	15	1,560	360	36
	25	870	320	90
9 ft./19%	1	4,590		
	2	18,400	5,800	18
	3	13,100	3,600	38
	7	5,820	1,700	112
	10	8,600	1,400	215
	15	2,700	1,300	215
	25	1,500	930	400
12 ft /24%	1	42,300	64	18
	2	45,100	3,000	11
	3	81,500	4,900	125
	7	14,000	4,160	750
	10	10,000	3,800	950
	15	5,400	2,280	1,030
	25	2,500	1,360	930

MB (ppm) applied Oct. 29, 1969†				
Depth and P_w*	Days after applic.	Lateral distance from application point (ft.): 2	5	8
1 ft /10%	3	264	147	
	5	253	234	
	7	157	249	
	12	71	200	
	24	lost	lost	
	33	23	61	
3 ft./12%	3	2,630	530	
	5	1,760	780	44
	7	1,120	830	155
	12	863	630	156
	24	310	270	
	33	230	160	
6 ft/13%	3	22,200	4,420	88
	5	15,000	6,190	370
	7	22,200	4,230	320
	12	4,170	2,880	580
	34	1,670	1,360	170
	33	1,000	860	
	40	780		
9 ft /20%	3	39,000	11,700	15
	5	32,300	11,000	37
	7	20,500	10,900	50
	12	9,470	4,740	860
	24	3,400	2,720	340
	33	2,440	1,710	
	40	1,760		
12 ft /20%	3	1,850	410	140
	5	35,300	880	170
	7	lost	2,200	190
	12	8,500	4,310	400
	24	5,170	3,400	1,220
	33	3,800	2,500	680
	40	2,500		

* P_w is weight per cent moisture in the soil horizon

† All blanks in table: samples analyzed, concentration MB was nil or trace

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[a] Kolbenzen et al., 1974

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controlling Armillaria mellea, oak root fungus, which often affects deep rooted perennial crops in California, such as grapes and citrus fruit.

4. Food and Feed

Monitoring efforts on foodstuffs and feed have been directed at examining residual amounts of bromomethane used as a fumigant after the target pest has been exterminated and the edibles released for consumption. In the literature examined, bromomethane (and its decomposition products) is the only monohalomethane which has been monitored in edibles.

In a study of a freight car and the hold of a ship bearing insect infested peanuts, Monro et al. (1955) found that loss of fumigant to the outside air could be kept to negligible levels. Loss of fumigant from the enclosed air-space was shown to be mainly due to absorption of the fumigant (bromomethane) by the peanuts themselves (rather than by the jute bag containers in which they were packed). The fate of the bromomethane absorbed by the peanuts was not considered.

Cows fed grain which has been fumigated with bromomethane give milk with bromide levels proportional to the amount of fumigated grain in their diet (Lynn et al., 1963). Table 25 shows the total bromide found in the fumigated grains and monitored in the milk where one pound of grain was fed for every four pounds of milk produced. Total blood bromides correlated with total milk bromides. Diets containing up to 43 ppm inorganic bromide from bromomethane residues resulted in 10 - 20 ppm bromide in the milk. The presence of bromide ion in the diet at the concentration levels investigated had no observable effect on milk production.

Bromomethane residues were determined in milled wheat products in which the wheat had been fumigated with bromomethane prior to milling

Table 25. Total Bromide (ppm) Monitored in Cow's Milk from Fumigated Feed [*]

In Grain	In Milk
53	4 - 12
100	7 - 12
220	10 - 20

[*] Lynn _et al_., 1963

(Shuey _et al_., 1971). Those wheat fractions in the exterior portions of the kernel and those with the highest fat content contained the most fumigant residue. The milling and baking properties of the flour were not affected by the fumigation. The fumigant treatment and residues found in four wheat types are given in Table 26. Fumigants are widely used in the food industry for controlling pests (Shuey _et al_., 1971), but information was not available as to how much, if any, bromomethane is actually in finished food products offered for human or animal consumption.

Table 27 summarizes monohalomethane monitoring efforts discussed in this section.

Table 26. Residue in ppm of Bromide in the Various Mill Fractions*

Variety	Treatment[a]	Bran	Shorts	Low Grade	Flour
Chris	A	<5	<5	<5	<5
	B	28	63	18	10
	C	32	66	19	10
	D	60	101	28	11
	E	55	111	35	11
Justin	A	<5	<5	<9	<5
	B	31	54	16	6
	C	37	75	19	7
	D	57	95	29	12
	E	62	111	37	10
Scout	A	10	7	7	8
	B	39	47	18	15
	C	36	55	21	15
	D	54	79	33	20
	E	61	89	34	20
Seneca	A	<5	<5	<5	<5
	B	28	52	28	7
	C	24	62	28	8
	D	38	93	48	14
	E	48	90	57	19

[a] A, Control; B, 1.5 lb. methyl bromide per 1,000 cu. ft., 28.9% r.h.; C, 1.5 lb. methyl bromide per 1,000 cu. ft., 81.9% r.h.; D, 3.0 lb. methyl bromide per 1,000 cu. ft., 34% r.h.; E, 3.0 lb. methyl bromide per 1,000 cu. ft., 86% r.h.

* W.C. Shuey et al., 1971

Table 27. Monohalomethane Monitoring in the Environment

Subject	Location	Halomethane	Concentration	Reference
Atmosphere	Atlantic Ocean	Iodomethane	1.2×10^{-12} v/v	Lovelock *et al.*, 1973
Atmosphere	New Brunswick, N.J.	Iodomethane	0.08 ppb	Lillian and Singh, 1974
Atmosphere	Pullman, Washington	Chloromethane	530 ppt	Grimsrud and Rasmussen, 1975
Atmosphere	Pullman, Washington	Bromomethane	<5 ppt	Grimsrud and Rasmussen, 1975
Atmosphere	Pullman, Washington	Iodomethane	<5 ppt	Grimsrud and Rasmussen, 1975
Atmosphere	Coastal waters, southern England	Chloromethane	$\sim 1.5 \times 10^{-9}$ v/v	Lovelock, 1975
Atmosphere	San Francisco, Calif.	Chloromethane	952.9 ppt	Singh *et al.*, 1977
Atmosphere	San Francisco, Calif.	Bromomethane	41.4 ppt	Singh *et al.*, 1977
Atmosphere	San Francisco, Calif.	Iodomethane	2.4 ppt	Singh *et al.*, 1977
Atmosphere	Kenya, Africa	Iodomethane	2.9×10^{-9} v/v	Block *et al.*, 1977
Fresh waters	Misc.	All except fluoromethane	NA	EPA (see Table 20)
Ocean	Atlantic, Caribbean, Antarctic	Iodomethane	135×10^{-12} ml/ml[a]	Lovelock, 1975
Ocean	Seashore, Dorset, Eng.	Chloromethane	11×10^{-9} ml/ml[a]	Lovelock, 1975
Ocean	Seashore, Dorset, Eng.	Bromomethane	2.4×10^{-9} ml/ml[a]	Lovelock, 1975
Ocean	Seashore, Dorset, Eng.	Iodomethane	1.8×10^{-9} ml/ml[a]	Lovelock, 1975
Tap water	Central Iowa	Bromomethane	2 ppb (av.)	Richard and Junk, 1977
Soil	California	Bromomethane	NA	Kolbezen *et al.*, 1974
Peanuts	Ontario	Bromomethane	NA	Monro *et al.*, 1955
Milk	East Lansing, Mich.	Bromide residues	10-20 ppm max.	Lynn *et al.*, 1963

NA = not applicable or data not available

[a] ml of vapor/ml of water

III. HEALTH AND ENVIRONMENTAL EFFECTS

A. Environmental Effects

1. Ecological Role of Monohalomethanes

Several investigators have suggested that chloromethane, bromomethane, and iodomethane presence in the environment can be clearly attributed to natural sources (Lovelock, 1975; Grimsrud and Rasmussen, 1975; Singh et al., 1977). These investigators have detected concentrations of the three compounds that far exceed quantities that could be explained by anthropogenic sources. Lovelock (1975) has suggested that a major source of chloromethane may be microbial fermentation (Cowan et al., 1973) and smouldering and combustion of vegetation (Lovelock, 1975 estimates that 1% of the chlorine content of vegetable matter is converted to chloromethane). The recent results of Singh et al. (1977) confirm that the ocean is probably the source of chloromethane and iodomethane and has a distinct effect on the concentration of bromomethane that is detected. Fluoromethane has not been detected in any ambient monitoring studies.

In the initial study by Lovelock et al. (1973) where iodomethane was first detected in air and seawater samples, the authors suggested that iodomethane "is the natural carrier of iodine between the seas and the land fulfilling a role for this element similar to that proposed for sulphur by dimethyl sulphide." Zafiriou (1975) has examined possible seawater-iodomethane interactions in order to better understand if iodomethane is the principal species of iodine entering the marine atmosphere. By comparing the rate constants for hydrolysis of iodomethane, chloride ion attack of iodomethane (determined experimentally), and the transfer of iodomethane to the atmosphere, Zafiriou (1975) concluded that some iodomethane will exchange into the atmosphere and some will react with seawater to form chloromethane. Thus, the iodomethane that does evaporate may be a natural carrier of iodine. Zafiriou (1975) also demonstrated that the iodine enrichment in sea-salt particles in the ocean atmosphere could not be explained by iodomethane evaporation, dissolution in droplets, and release of iodine by chlorine ion exchange.

The question of whether monohalomethanes, especially chloromethane, are stable enough to diffuse to the stratosphere and affect the stratospheric ozone has been a matter of lively debate. Lovelock (1975) has suggested that naturally occurring chloromethane may diffuse to the stratosphere and act as a natural regulator of stratospheric ozone. Rowland _et al_. (1975) agreed that the stratospheric ozone may be regulated by halogenated methanes including chloromethane but indicated that the depletion of ozone due to anthropogenic chlorine is almost independent of the destruction due to natural chlorine sources. The calculations of Robbins (1976) indicate that, up to an altitude of 10 km, atmospheric transport to higher elevations is the dominant loss mechanism for either chloromethane and bromomethane. Although bromomethane is not as prevalent a natural product as chloromethane and is about 10% less stable to oxidation with OH radical (Robbins, 1976), Wofsy _et al_. (1975) have suggested that bromine radicals may be even more efficient catalysts for ozone destruction than either nitric oxides or chlorine. His calculations suggest that bromine may cause a 0.3% reduction in global O_3 concentration, of which 0.2% may be attributed to bromomethane (Wofsy _et al_. 1975, suggest that only 5-25% of the bromomethane is from anthropogenic sources; Hunt 1977, estimates that only 0.8% is from anthropogenic sources). Resolution of this potential ecological effect will require a better understanding of stratospheric chemistry and perhaps some stratospheric monitoring for the monohalomethanes.

Macon et al. (1971) have examined the possibility of iodomethane reaction with mercury salts in aqueous drops to form organomercury pollutants. Because only one mercury form (C_2H_5HgI) was identified, the authors were unable to conclude the environmental implications of such a reaction. Wang et al. (1976) have evaluated the "greenhouse effects" of a number of trace gases including chloromethane. Chloromethane had a relatively minor greenhouse effect compared to some of the other gases examined, such as trichlorofluoromethane and dichlorofluoromethane.

In summary, there is a considerable amount of information that indicates that chloromethane, bromomethane, and iodomethane are natural environmental constituents. However, their ecological role, if any, is poorly understood.

2. Persistence

The fact that chloromethane, bromomethane, and iodomethane have been detected in ambient air and water samples indicates that these compounds possess some stability in the environment. Based upon bond energies (see Section I-A-1), one would expect that the stability would decrease in the order F>Cl>Br>I. Although the experimental data is somewhat limited, the environmental persistence of monohalomethanes appears to follow the above order.

In the atmosphere, oxidation (Section I-B-2) and photolysis (Section I-B-3) are important processes for the degradation of monohalomethanes. A number of investigators have suggested residence times, which are usually based upon monitoring data, and half-lifes, which are usually based upon experimental data or theoretical calculations. Lovelock et al. (1973), who were the first investigators to detect iodomethane, indicated an atmospheric residence time of 0.003 years based upon some unpublished work by Eggleston and Clough which indicated a residence time of 50 hours. Singh et al (1977) also suggest a low atmospheric stability for iodomethane, stating that iodomethane "is easily photolyzed in the tropospheric sunlight with a half-life of less than 2 days."

Chloromethane is considerably more stable than iodomethane. Singh et al. (1977) indicate that chloromethane has a tropospheric lifetime of less than one year. Lovelock and coworkers (Lovelock, 1975; Cox et al., 1975) have indicated that the rate of reaction of chloromethane with OH radical in the troposphere would indicate a residence time of 0.37 years if that reaction were the sole sink. Spence et al. (1976) have studied the photooxidation of chloromethane in dry air using the photolysis of molecular chlorine to initiate the oxidation of the halocarbons studied. Oxidation of chloromethane resulted in formyl chloride ($HCOCl$) as the principal product as well as hydrogen peroxide, carbon monoxide, and hydrogen chloride. Under real atmospheric conditions, the oxidation would be initiated by OH radical, but the main products would still be those noted above.

Robbins (1976) has compared the rate of loss of chloromethane and bromomethane at various altitudes by one of three mechanisms: (1) diffusion (transport to higher elevations), (2) reaction with OH radical, and (3) photodissociation. Table 28 summarizes his results which are depicted in Figure 10. The OH radical reaction rates with chloromethane and bromomethane were assumed to be $1.69 \times 10^{-12} \exp(-1066/T)$ cm^3/sec and $8.3 \times 10^{-13} \exp(-914/T)$ cm^3/sec, respectively.

The persistence of monohalomethanes in natural waters has received only limited attention even though chloromethane, bromomethane, and iodomethane have been detected in seawater (Lovelock, 1975) and other ambient and drinking water samples (see Section II-E).

Table 28. Comparison of Photodissociation, Diffusion[a], and OH Oxidation Rates of Chloromethane and Bromomethane in the Atmosphere[b]

Altitude Kilometers	CH_3Cl	CH_3Br
0-10 (troposphere)	Diffusion dominant mechanism	Diffusion dominant mechanism
∿12 (lower stratosphere)	OH radical reaction and diffusion equal; no photodissociation	OH radical reaction and diffusion equal
>25	OH radical reaction fastest; no photodissociation	Photodissociation faster than other mechanisms
30	Three mechanisms about the same	Photodissociation major mechanism

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[a] Diffusion actually references to atmospheric transport to higher elevations resulting in dilution and, thus, a "loss."

[b] Robbins, 1976

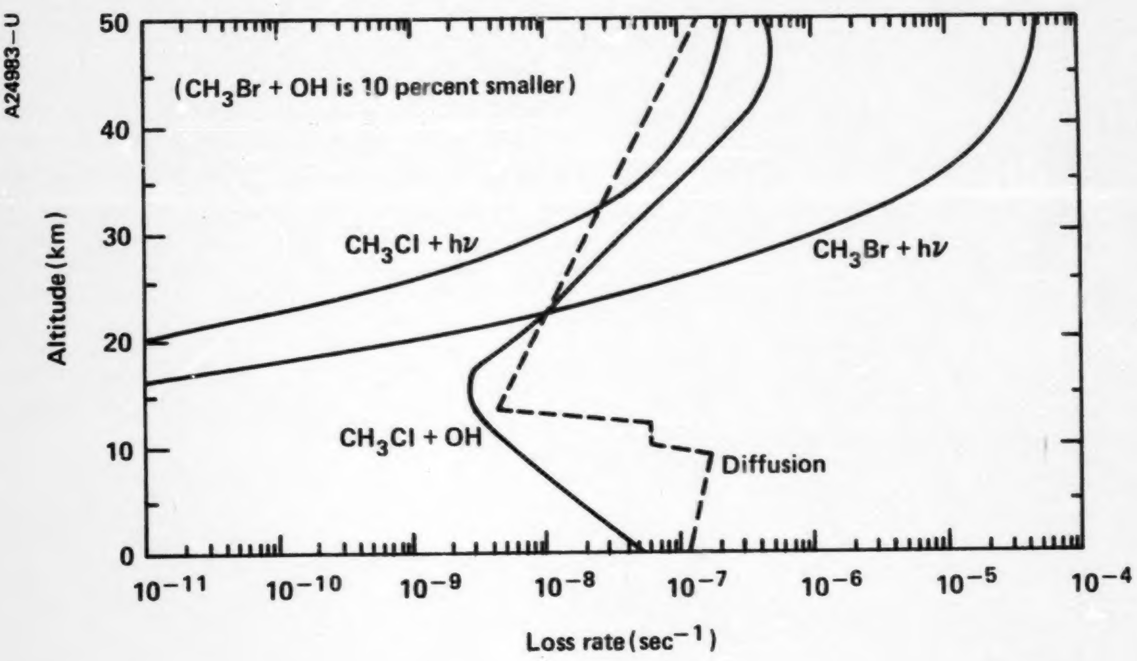

Figure 10. Loss Rates of CH_3Cl and CH_3Br, Reaction with OH, and Diffusion as a Function of Altitude (Robbins, 1976) (Photodissociation Rates are for Solar Zenith Angle of 60° at 30° Latitude)

Zafiriou (1975) has determined the rate of disappearance of iodomethane in seawater by analyzing the decreasing iodomethane concentration at various times using gas chromatography. The experimental rates in seawater or NaCl solutions were compared with calculated hydrolysis rates for iodomethane and chloromethane in water (Table 29). These results indicate that iodomethane reacts rapidly (half-life of 0.054 year) with the chloride ion in seawater but would probably be considerably more stable in non-brackish water. Zafiriou (1975) calculated that the reaction of iodomethane with bromide ion would be 0.12 as reactive as reaction with water and 0.013 as reactive as reaction with chloride ion.

The calculated rates of hydrolysis in water compare well with the values reported by Heppolette and Robertson (1959) (Table 7). However, the calculated rate constants are for neutral pH water, and since hydrolysis reactions are pH dependent, especially under alkaline conditions, exact agreement should not be expected. Fells and Moelwyn-Hughes (1959) have reported some reaction rates for monohalomethanes with hydroxyl ion in water at 100°C. These rates are generally faster than under neutral conditions at comparable temperatures.

With the exception of some data for bromomethane, little information is available on the persistence of monohalomethanes in soil. The information on bromomethane results from its use as a soil fumigant. Abdalla _et al_. (1974) have measured the concentration of bromomethane in the "soil atmosphere" at various depths in several different soils. In most cases, bromomethane was detectable 14 days after treatment; similar results have been reported by Kolbezen _et al_. (1974) (see Table 24, p. 92). Van Wambeke (1974) have studied the factors that affect bromide residues in soil after bromomethane fumigant treatment. This formation of bromide from bromomethane in soil is well known, but the mechanism and rate of degradation has not been studied.

Table 29. Rates of S_N2 Reactions of Monohalomethanes in Water[a]

Halide	Nucleophile	T,°C	K´(sec^{-1})*	Half-Life (yr)
CH_3I	Saturated NaCl	19.2	4.0×10^{-6}	0.0055
		10.8	7.3×10^{-7}	0.030
	19.0^{0}/00 Chlorinity NaCl	19.2	3.5×10^{-7}	0.062
	19.8^{0}/00 Chlorinity Sea Water	19.2	4.1×10^{-7}	0.054
		10.8**	1.4×10^{-7}	0.16
	Water (Calc.)	0	9.4×10^{-10}	23
	Water (Calc.)	10	5.4×10^{-9}	4.0
	Water (Calc.)	20	3.2×10^{-8}	0.69
CH_3Cl	Water (Calc.)	0	2.5×10^{-10}	88
	Water (Calc.)	10	1.6×10^{-9}	14
	Water (Calc.)	20	8.9×10^{-9}	2.5

* Pseudo first-order rate constant.

** Over initial 42% of decay.

[a] Zafiriou, 1975

3. Bioaccumulation and Biomagnification

The high vapor pressure of the monohalomethanes and relatively high water solubility (compared to chemicals such as DDT) indicate that the monohalomethanes have a low potential for bioconcentration. Using the water solubilities (CH_3Cl = 5380 ppm; CH_3Br = 1000 ppm and CH_3I = 14000 ppm) and the equation of Metcalf and Lu (1973), the biomagnification factor is two, six, and one, respectively.

4. Biological Degradation

No information is available on the biodegradability of monohalomethanes by microorganisms. However, Colby *et al*. (1975) have shown that extracts of *Methylomonas methanica* catalyze the disappearance of bromomethane from reaction flasks only in the presence of O_2 and NADH.

5. Environmental Transport

The high vapor pressures of all of the monohalomethanes and the fact that only one compound (iodomethane) is a liquid (the rest are gases) at ambient conditions indicate that evaporation and diffusion are important transport processes. Considerable evidence suggests that chloromethane, bromomethane, and iodomethane are naturally present in seawater. Dilling (1977) has experimentally measured the half-life for evaporation from water of a number of chlorocarbons, including chloromethane, and has compared the results to a calculated half-life. The experimental values were in good relative agreement with the calculated values. The chloromethane calculated half-life for a depth of 6.5 cm was 26.5 minutes (K_1 = 0.170 cm min^{-1}) while the experimental half-lifes were averages of 27.1, 25.4, and 20.2 minutes. Assuming the same depth, iodomethane has a half-life of 42.9 min. Zafiriou (1975) has indicated that some iodomethane that is formed in seawater will evaporate and some will react with chloride ion in seawater, and then the chloromethane which is formed will evaporate much faster than the iodomethane. Some bromomethane may be formed and evaporated in a similar fashion, although the quantity formed will be considerably smaller because bromide ions react about 0.01 as fast as chloride ions.

After evaporation from water, horizontal transport of monohalomethanes in the atmosphere takes some time as indicated by the different concentrations detected in the atmosphere near seawater compared to air sampled inland (Singh et al., 1977). Iodomethane appears to degrade rapidly in the troposphere, while chloromethane and bromomethane both appear to diffuse (dilution by atmospheric transport) faster than they react with OH radicals or are photodissociated (Robbins, 1976). As the two compounds diffuse upward, degradation processes begin to compete with diffusion (see Sec. III-A-2 and Figure 10). Because of their high volatility and low water solubility in water, washout mechanisms that would bring the compounds back to soil or water do not seem to be very important. However, bromomethane might be condensed in cold regions since it becomes a liquid at 3.56°C. Wofsy et al. (1975) have noted that bromomethane has been detected in antarctic snow.

Wildung et al. (1974) have measured the distribution coefficient (K_d) of iodomethane with soil. The distribution coefficient was defined as the ratio, at equilibrium, of the quantity of solute sorbed per gram of soil to solute per ml of equilibrating solution. The K_d values for iodomethane ranged from 0.1 to 3.1 depending upon the soil. A positive correlation to clay, organic carbon, and cation exchange capacity and a negative correlation to pH of the soil was noted. The authors concluded that in surface soils containing sufficient clay and organic matter, iodomethane has the potential for accumulation.

Much of the bromomethane that is applied as a fumigant to soil, grain, seed, etc. evaporates (estimates of 25-50% have been given, Wofsy *et al*. 1975; Hunt 1977, feels 5 to 10% is a more reasonable figure). When soil injection is used, a polyethylene tarp is placed over the soil to reduce evaporation. A number of factors including moisture and soil type affect the amount of penetration into the soil (Kolbezen *et al*., 1974). Following injection, the bromomethane gas can penetrate vertically or laterally (see Table 24 in Section II-E).

B. Biological Effects

Bromomethane has been widely used for over 30 years as a fumigant for the control of insects, mites, and invertebrate pests which infest stored harvested produce and processed foods. Because of this use, considerably more biological effects data are available for bromomethane than are available for the other monohalomethanes.

1. Toxicity and Clinical Studies in Man

a. Symptoms of Exposure

Bromomethane and chloromethane are among the substances that can closely imitate alcohol intoxication. Exposure to both chemicals produces neurologic symptoms such as slurred speech, slow response, poor memory, unsteady gait, and behavioral modifications (Eckardt, 1971). Exposure to bromomethane via fire extinguishers is not likely anymore, as it is no longer utilized in that capacity. However, bromomethane fumigation of crops, dwellings, and foodstuffs is still widely practiced.

Bromomethane

The symptoms of bromomethane poisoning vary somewhat, depending upon whether the liquid bromomethane comes in direct contact with the skin or whether the fumes are inhaled. The following is a capsulated summary of bromomethane poisoning effects gleaned from studies cited by von Oettingen (1964), Kleinman *et al*. (1960), Rathus and Landy (1961), Drawneek *et al*. (1964), Longley and Jones (1965), Hine (1969), Greenberg (1971), Araki *et al*. (1971), Mizyukova and Bakhishev (1971), Pereira and Almeida (1971), Mellerio *et al*. (1974), and Shapovalov (1974). Direct contact of the skin with bromomethane may cause prickling and itching in addition to the initial cold sensation. This is followed by erythema, vesication, and blister formation which may be more severe if clothing is present, particularly binding wearing apparel such as shoes. The blisters which appear resemble second degree thermal burns. Where exposure is insufficient to cause blisters, a fine, papular, vesicular, itching dermatitis frequently develops after a latent period of up to several days.

Fatal exposures are followed by a latent period of from 30 minutes to 48 hours before symptoms develop. Early signs of bromomethane poisoning are malaise, headache, visual disturbances, nausea, and vomiting. Tremors and twitchings are frequent and are followed by convulsions and then periods of unconsciousness. The patient has a variety of psychic feelings following exposure and before the onset of convulsions. They may be confused, disoriented, agitated, euphoric, depressed, or delirious. The convulsions are of the Jacksonian type, with the tremor starting at one extremity and then becoming generalized. Initially, the pulse is normal and the skin is flushed. As respiratory stress increases, the skin appears cyanotic and the pulse is fast and thready. As pulmonary edema develops, the blood becomes more concentrated, as indicated by the presence of polyglobulinemia, hyperchromasia, elevated hemoglobin, albuminuria, uremia, and, in some cases, leukocytosis. Death usually occurs during a convulsion seizure.

In cases of bromomethane poisoning which can be considered acute-transient (Araki _et al_., 1971), the victim first experiences vertigo, lassitude, somnolence and headache, all of which usually disappear in a few days. Unsteadiness of gait is present and, even in such cases as these, occasional extrapyramidal symptoms and temporary myoclonus are experienced. Additional nervous symptoms may be expressed as gastrointestinal disturbances, such as anorexia, nausea, vomiting, and diarrhea.

In cases of bromomethane poisoning which may be classified as acute-severe (Araki et al., 1971), the headaches become violent; cerebellar and labyrinthal disturbances are marked; myoclonus, tremors, and even epileptiform convulsions are present. The victim may suffer asthenia and ataxia, and some patients have disturbances of the reflexes. Blurred vision, diplopia, and sometimes temporary blindness are common. Recovery is usually complete, although in some cases permanent brain damage is encountered (Drawneek et al., 1964; Greenberg, 1971; and Mellerio et al., 1973).

Chloromethane

A summary of the characteristics of chloromethane exposure can be derived from von Oettingen (1964), MacDonald (1964), and Spevak et al. (1976). Symptoms vary with the intensity of the exposure. In fatal poisonings, the victims suffer nausea, vomiting, colicky pain, and diarrhea. Later, severe headaches, vertigo, slurred speech, confusion, drowsiness, and loss of equilibrium develop. Finally, the patient loses consciousness and passes into a coma. The pulse becomes rapid, respirations are rapid, and the breath usually has a sweetish and offensive odor. Some victims develop renal damage resulting in oliguria and anuria. Others develop anemia with anisocytosis, achromia, and mild leukocytosis.

Less severe cases of chloromethane poisoning also present the symptoms of nausea, vomiting, anorexia, colicky pain, diarrhea, drowsiness, headache, vertigo, incoordination, tremors of hands and lips, ptosis of the eyelids, and nystagmus. Some individuals express liver injury as jaundice and porphyrinuria, and renal disturbances characterized by albuminuria and oliguria which may pass into anuria. Nervous disturbances are very common and may be severe. The reflexes may be hyperactive and pathological reflexes (Babinski) may be present. Tremors, muscular twitchings, and clonic-tonic convulsions with opisthotonos and trimus may develop. Restlessness, mental confusion, euphoria or depression, morbidness, anxiousness, and mental instability are all possible symptoms. Complete recovery from chloromethane poisoning may take months, and in some cases permanent personality and central nervous system changes may occur.

Iodomethane

Symptoms of human exposure to iodomethane reported by von Oettingen (1964) include giddiness, somnolence, double vision, vomiting, and diarrhea. Later effects included slurred speech, restlessness, irritability, manic conditions, and spells of unconsciousness. Skin exposure results in bullous dermatitis (Devine, 1964). Appel et al. (1975) noted paranoia and periods of catatonic posturing.

Fluoromethane

No data are available.

b. Poisoning Incidents and Case Histories

Bromomethane

Von Oettingen (1964) reported that at least 56 fatalities occurred between 1899 and 1962, the majority of which resulted from exposures to bromomethane from leaking fire extinguishers. The remaining fatalities occurred during chemical handling operations and from its use in fumigations. The fatal exposures were reported at levels ranging from 300 to 60,000 ppm. Since 1964, lethal exposures to bromomethane have been reported to have caused four deaths in California as the result of workers fumigating foodstuffs (Hine, 1969). Two deaths were reported in France between 1964 and 1974 (Mellerio et al., 1974), and a six-year-old boy died after entering a fumigated warehouse in Japan (Kashima et al., 1969). While this probably does not represent all the lethal exposures to bromomethane, it clearly indicates that uses of the chemical and casual exposure to non-users need to be carefully controlled. As will be described below, non-lethal exposures to bromomethane can have permanent effects on the victims.

Butler et al. (1945) reported the case of two men exposed to bromomethane liquid when a fire extinguisher filled with four pounds of bromomethane was used to put out a fire in the dashboard of an armored car. They continued their trip for another five hours after their feet were soaked in the bromomethane. Large blisters were present on the feet and calves of both men, the largest being 4 inches by 5 inches. Three different treatments were applied: 2% tannic acid in triple dye solution; propamidine cream; and calcium pencillin powder. All promoted satisfactory healing. The individual with the least severe bromomethane blisters was released in 14 days with all blisters healed. The second individual was retained for eight weeks before discharge. Although no other symptoms or effects were noted, this individual's feet were healed in two weeks with only a secondary eruption occuring at five weeks. No mention of blood chemistries or alterations in behavior were made by the authors.

Longley and Jones (1965) reported the case of a man sprayed with bromomethane from a leaky fire extinguisher which he was filling. The patient decontaminated himself within three minutes and no blisters developed. However, five hours later twitching in his right arm started and his physical state deteriorated over the next few hours with recurrent fits. Permanent brain damage resulted involving the pyramidal tracts, as well as the cerebellum. Anticonvulsive therapy was necessary because convulsions developed upon withdrawal of the drugs.

Hine (1969) reported a total of 166 cases of bromomethane poisoning in California between 1957 and 1964. Sixty-two had systemic poisoning; five deaths were reported; and 99 other cases of unspecified dermatitis, burns, or other minor irritations were reported. In this report, the author reviewed ten cases involving bromomethane, four of which were fatal. In a discussion of the significance of the blood bromide level, Hine (1969) agrees with Rathus and Landy (1961) that bromide levels of 400 ppm resulted in gross disability; 250 ppm in convulsive seizures; 175 ppm in slight residual ataxia; 135 ppm in moderate disability; and 100 ppm and less in complete recovery.

Chloromethane

Up to 1962, at least 21 fatalities had been reported due to chloromethane poisoning (von Oettingen, 1964). A review of the literature since that time has failed to find additional fatalities. Neither the minimal fatal nor the minimal toxic dose of chloromethane for man has been determined; however, acute poisoning occurs from exposures above 500 ppm. Most of these poisonings resulted from leaking domestic refrigerators or from defects in refrigeration plants.

Prior to 1962, at least 241 nonfatal cases of chloromethane poisoning were reported (von Oettingen, 1964). Since then, at least 34 cases have been reported (MacDonald, 1964; Spevak _et al_., 1976). Again, exposures were primarily the result of a faulty refrigeration system utilizing chloromethane as the coolant. Spevak _et al_. (1976) reported the case of four members in one family exposed to chloromethane leakage from a domestic refrigerator. All victims had symptoms of central nervous system involvement and kidney injury. Three of the victims were jaundiced and had increased bilirubin levels, serum creatinine, blood urea, and proteinuria. The kidney damage disappeared in two weeks and all four recovered completely. Table 30 is a summary of the neurologic and psychic disturbances present in these four individuals.

Iodomethane

Only two cases of fatalities due to iodomethane exposure were reported by von Oettingen (1964). Appel et al. (1975) reported that only six cases of iodomethane poisoning were present in the literature, and the only other report in the English language that they found was that of Garland and Camps in 1945 (Appel et al., 1975). However, an extensive search of the literature produced one other report in which iodomethane was implicated (Devine, 1964).

The case of iodomethane poisoning in a 41-year-old male chemist producing large quantities of iodomethane in his home laboratory was reported by Appel et al. (1975). Initially, he had blurred vision and an unsteady gait. Later he experienced double vision, became lethargic and confused with dysarthic speech and gross dysmetria of the upper extremities. During the first two days in the hospital, he was semistuporous, with prominent cerebellar findings. Serum iodine was 31 μg/100 ml, and cerebrospinal fluid iodine was 5.3 μg/100 ml. EEG showed diffuse slowing, with delta and theta activity not localized. Five weeks later, serum iodine was 6.5 μg/100 ml, and uptake of radioactive iodine was only 4% (3% on admission). Repeat EEG's were progressively more organized. For periods of time, the patient would assume catatonic posturing, be paranoid, and require help to walk. The clinical picture was one of an individual with a serious organic impairment of intellectual functioning and personality organization. Five months after poisoning, the patient still

Table 30. Neurological and Psychic Disturbances in Four Members of One Family Exposed to Chloromethane*

Symptom	Sister			Brother
	1 (52 years)	2 (50 years)	3 (60 years)	64 years
Photophobia	+++	+	+	+
Mydriasis and anisocoria	++	++	++	++
Nystagmus	+	+	+	+
Weakened convergence	+	-	-	+
Strabismus	+	-	+	-
Diplopia	+	+	-	-
Paresis of facial nerve	+	+	+	+
Twitching of facial muscles	++	++	++	++
Hyperacusis	-	-	-	-
Pyramidal symptoms - hyperreflexia and elevated tonus	++	+	+	+
Tremor	++	++	++	++
Rombergism	+++	+++	++	+++
Adiadochokinesis	-	+	-	-
Sensitivity	-	+	+	++
Speech disturbances	++	+++	++	+
Consciousness, psychic disturbances	Somnolence, apathy, euphoria	Somnolence, euphoria	Somnolence	Somnolence

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* Spevak _et_ _al_., 1976

experienced paranoid feelings occasionally and admitted that his mind was not entirely clear when performing calculations.

Fluoromethane

No data are available.

c. Occupational Studies

Bromomethane

In the state of California in 1957 there were 749 reported cases of occupational exposure to pesticides, of which five cases were due to bromomethane exposure (Kleinman *et al.*, 1960). Rathus and Landy (1961) reported the cases of seven workers exposed to bromomethane fumes while fumigating houses. Of these seven men, three completely recovered within a month. The remaining four had permanent changes. The least affected individual had a slight residual ataxia, while another individual developed grand mal epilepsy and periods of hysteria. The remaining two individuals had permanent central nervous system damage. In one individual, the left pupil reacted slowly to light; he had an intention tremor in the left hand; and heel-toe walking was unsteady. He also experienced myoclonic jerks in the legs at night. The last individual was unconscious for seven days, and on discharge from the hospital after ten weeks was still grossly ataxic and still had recurrent Jacksonian motor attacks of the right leg and myoclonia of the right arm. Permanent changes in electroencephalogram were noted, and at two years post exposure this individual had the same signs as when discharged.

Drawneek *et al.* (1964) reported the case of a 47-year-old male who had been a fumigator for 14 years. This individual had permanent organic brain damage which expressed itself as difficulty in concentrating, depression, and increased physical weakness. Eleven other fumigators in the area were tested to determine the bromide level in the blood. Seven were found to have levels above 5 mg and to be mildly euphoric. This case report indicates that prolonged exposure to subacute levels of bromomethane may cause irreversible brain damage and that workers with a serum level of 5 mg bromide become euphoric.

Greenberg (1971), in addition to reporting on a 44-year-old male who developed permanent brain damage from fumigating cocoa beans, summarized the neurological effects of bromomethane poisoning. Greenberg (1971) felt that bromomethane can cause two types of neurologic syndromes depending on the duration and content of the exposure. It appeared that chronic, low-level exposure will result in a chronic polyneuropathy, whereas short exposure to high levels of bromomethane will result in headaches, dizziness, nausea, vomiting, generalized weakness, transient diplopia, seizures, and tremors. Paranoia and other mental symptoms develop and may persist. Convalescence may last up to 18 months with some residual permanent damage.

Araki *et al*. (1971) discussed 14 cases of bromomethane poisoning which they studied between 1964 and 1970. They report symptoms of poisoning as stated in Section III-B-1-a, p. 109. Their cases included 13 fumigators and one chemist who was manufacturing tribromosalicylanilide. They felt that the latent period before the onset of symptoms and the outcome seemed to be related to the quantity and duration of the exposure. Table 31 illustrates a clinical classification of bromomethane poisoning which may be used to simplify complicated clinical pictures due to poisoning. In this study, four cases were classified as acute-transient, two cases as acute-severe, and eight cases as chronic.

Table 31. A Clinical Classification of Bromomethane Poisoning*

Clinical Type		Latent Period	Clinical Manifestations	Outcome
Acute Poisoning	Transient type	Several minutes to several hours	Initial symptoms: headache, dizziness, nausea and vomiting, unsteadiness of gait	Complete recovery (within one month)
	Severe type	Several hours	Coma, generalized convulsion, ataxia of gait	Sequelae are usual
	Fulminant type	Within several hours	Acute pulmonary edema	Death (within 48 hours)
Chronic Poisoning		Over several months (repeated exposures)	Ataxia of gait	Improvement (more than several months later)

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* Araki _et al_., 1971

In a study on 113 fumigators of coffee grains in Brazil (Pereira and Almeida, 1971), 70% of the workers experienced clinical symptoms of intoxication similar to responses seen in bromomethane poisoning. Headaches, unsteady gait, blurred vision, and slurred speech were common. In addition to bromomethane, phosphine and malathion were used. Some workers applied more than one of the chemicals. However, symptoms were most frequently observed among persons who had predominantly applied bromomethane.

Chloromethane

MacDonald (1964) reported the histories of eight individuals in a synthetic rubber plant exposed to chloromethane at various concentrations from 25 to more than 10,000 ppm. Reactions of these eight individuals included blurring of vision, headache, and loss of coordination. Headaches were severe and occurred intermittently for seven to ten days. Nausea and vomiting occurred in the more severely intoxicated, but vomiting lasted only a few hours, and nausea for a few days. Personality changes occurred in six of eight patients, but were reversible in all but one patient who experienced a period of unconsciousness. These victims became depressed, morose, and anxious, except for one euphoric patient. Those patients who were exposed to moderate to severe doses of chloromethane were more sensitive to chloromethane on return to work. Blood tests conducted on the patients did not reveal any changes. According to this author, the best clue to making a diagnosis of chloromethane poisoning is the interview with the victim, as the symptoms mimic (among other things) endemic encephalitis, infective hepatitis, and incipient peritonitis.

Earlier reports of occupational contact with chloromethane support the observations that toxic actions in the central nervous system are a significant feature of clinical intoxication (Hansen _et al_., 1953; Browning, 1965; Morgan, 1942).

Iodomethane

Exposure to iodomethane in the workplace is much more limited than that of either bromomethane or chloromethane. The lethal dose is not known; however, based on animal studies (Section III-B-2), iodomethane should be considerably more toxic than either bromomethane or chloromethane.

Fluoromethane

No information of fluoromethane toxicity is available. Based on information available from the other three halomethanes, iodomethane would be the most toxic, followed by bromomethane, chloromethane, and then fluoromethane.

d. Metabolic and Physiologic Effects

Similarities in the clinical manifestations of poisoning by the monohalomethanes suggest a common mechanism of toxic action. It is known that with bromomethane and iodomethane, the halogen atom is released as the inorganic ion in the body (Morgan and Morgan, 1967; Miller and Haggard, 1943; Irish *et al.*, 1940, 1941). It is probable that the same reaction occurs with chloromethane *in vivo* (Redford-Ellis and Gowenlock, 1971 a). Evidence which is presented below, however, suggests that the halogen ion is not the mediator of toxicity, but rather the methylation of essential proteins leading to their inactivation may be responsible for clinical symptoms resulting from overexposure.

Bromomethane

Nearly 30 years ago, Lewis (1948) postulated that bromomethane reacted with sulfhydryl groups via the following reaction:

$$RSH + CH_3Br \longrightarrow RSCH_3 + HBr$$

Since many enzyme systems depend upon sulfhydryl groups in their biological action, the introduction of bromomethane could cause a progressive and irreversible inhibition. Lewis (1948) showed that the number of sulfhydryl groups decreases when buffered solutions of cysteine and reduced glutathione are heated with low concentrations of bromomethane, indicating a preferential reaction with sulfhydryl groups. Mizyukova and Bakhishev (1971) have found that the administration of cysteine has proven to be a highly efficient means of treatment for bromomethane intoxication. Lewis (1948) has also demonstrated that bromomethane inhibits urease, succinic dehydrogenase, papain, and yeast respiration. Dixon and Needham (1946) have found that hexokinase (a sulfhydryl-containing enzyme) which is present in the brain is strongly inhibited by bromomethane *in vitro*. These results suggested that inhibition of carbohydrate metabolism may be involved in the mechanism of bromomethane toxicity.

Shapovalov (1974), in a study on 140 workers, found liver, thyroid, and hematological changes following exposure to bromomethane, elementary bromine, and bromides. Additionally, alterations in carbohydrate metabolism with moderate hypoglycemia and pathological sugar curves of the irritative type were found. Lipid metabolism studies revealed hypercholesterolemia and a reduction in total bilirubin. Blood changes included a tendency towards anemization, thrombocytopenia, leukopenia, and enhanced erythrocyte sedimentation rate. The uptake of ^{131}I by the thyroid gland was inhibited. Many of these responses might be non-specific indicators of chronic exposure to bromomethane and bromine-containing compounds.

Mellerio *et al*. (1973, 1974) have studied seven cases of bromomethane poisoning, giving special emphasis to changes in electroencephalograms (EEG). They concluded that central nervous system changes may be diffuse or local. In two cases of mild bromomethane exposures, there were no changes in EEG. In the remaining five cases, one case had a transitory abnormality and the other four had major alterations in their EEG. These changes showed a permanent and areactive slowing of activities and paroxysmal diffuse activities of long duration which were resistant to therapy (Hemineurine, diazepam, and barbiturate). Other reports (Araki _et al_., 1971; Greenberg, 1971; Longley and Jones, 1965; and Hine, 1969) had reported changes in EEG, but the report by Mellerio _et al_. (1973) gives a detailed description of changes found in their cases.

Chloromethane

Redford-Ellis and Gowenlock (1971 a) have shown that chloromethane reacts with human plasma and erythrocytes. Using $^{14}CH_3Cl$, most of the plasma radioactivity was found to be bound to sulfhydryl groups of albumin. On hydrolysis, the major reaction product was S-methylcysteine (98.4%). Small amounts of 1- and 3-methylhistidine were also found (1.2 and 0.8%, respectively). In plasma, the bound radioactivity corresponds to only 2 to 3% of the uptake using unlabelled CH_3Cl, suggesting that other, unidentified volatile products are formed. In erythrocytes, approximately 40% of the uptake was bound by reduced glutathione (GSH), forming S-methylglutathione. The reaction appears to be catalyzed by an enzyme in the erythrocytes, since chloromethane did not react with GSH in saline or plasma. Loss of thiol groups from plasma protein and erythrocytes, and inhibition of oxygen uptake by erythrocytes were not observed, thus making the generalization that chloromethane inhibits all GSH-dependent enzymes untenable. The inhibition of glyoxalase by S-methylglutathione has been established, and the possibility exists that other GSH-dependent enzymes might be affected by chloromethane. Anemia is a fairly common response to chloromethane. It is tempting to suggest that those individuals exposed to chloromethane also had a decrease in erythrocyte GSH, leading to anemia.

Iodomethane

Morgan and coworkers (Morgan *et al.*, 1965; Morgan and Morgan, 1966; Morgan and Morgan, 1967; Morgan *et al.*, 1967) have studied the effects of inhaled iodomethane, since small amounts of iodomethane are released from uranium fission reactors. In a group of volunteer subjects, at normal breathing rates, the retention of radioactive iodomethane varied from 53 to 92% (mean = 72%), depending upon the number of breaths per minute. The lung clearance of inhaled iodomethane was calculated at 2.2 seconds. Uptake by the thyroid of iodomethane accounted for about 20% of the iodomethane after five hours. Urinary excretion of the ^{131}I was rapid with 40% of the retained activity eliminated by ten hours. After inhalation, the concentration of ^{131}I in venous blood rises very rapidly initially, and then more slowly, until the maximum concentration is reached at 10 to 30 minutes after exposure. At this time, about 20% may be accounted for in the circulating blood. Figures 11 and 12 depict the uptake by the thyroid, urinary excretion, and venous blood levels of ^{131}I after inhalation of iodomethane. The authors attempted to compare the metabolism of iodine introduced by the inhalation of iodomethane with that of the ingestion of iodine as sodium iodide. They concluded that the metabolic pattern of iodine, introduced by the inhalation of iodomethane, is the same as that of the iodide ion (see Figure 13). They suggested that iodomethane is rapidly broken down and releases the iodide ion. The site and mechanism of the demethylation process was not established.

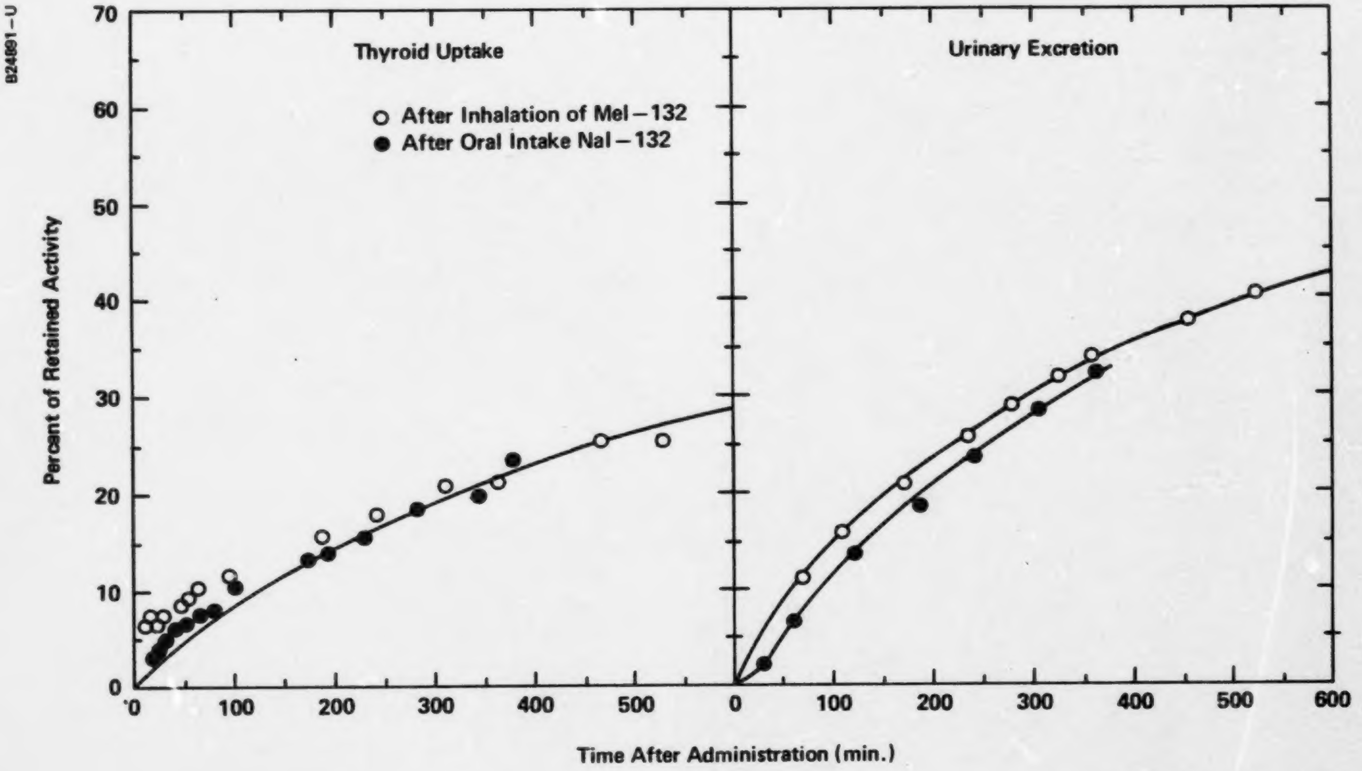

Figure 11. Comparison of Thyroid Uptake and Urinary Excretion of Iodine-132 After Inhalation as Iodomethane and Ingestion as Sodium Iodide (Morgan et al., 1965)

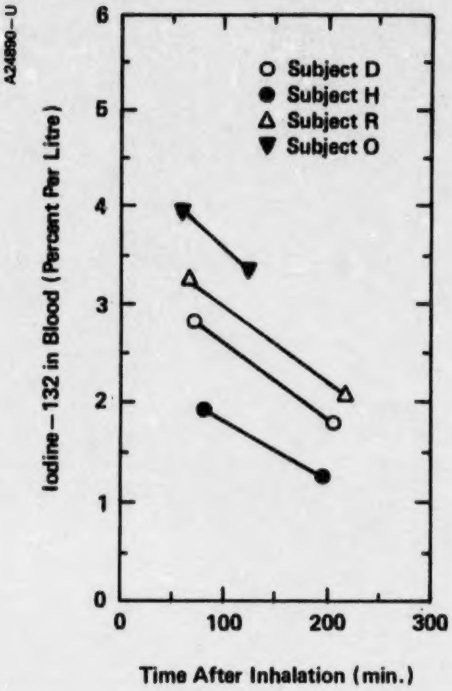

Figure 12. Concentration of Iodine-132 in Venous Blood After Inhalation of Labelled Iodomethane (Morgan _et al_., 1965)

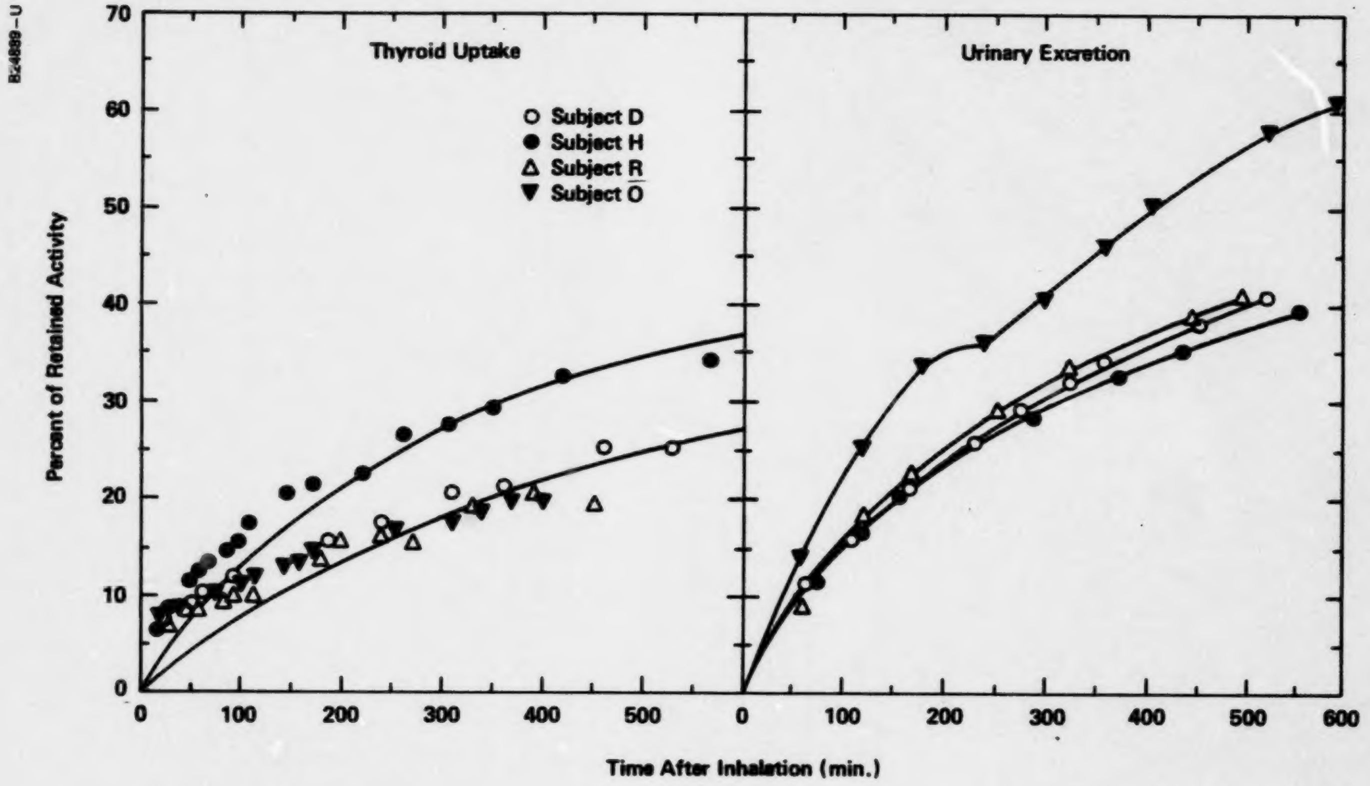

Figure 13. Thyroid Uptake and Urinary Excretion of Iodine-132 After Inhalation of Labelled Iodomethane (Morgan et al., 1965)

Fluoromethane

No data are available.

e. Epidemiology

There are no data in the published literature regarding retrospective or population studies of humans exposed to the monohalomethanes.

2. Biological Aspects in Non-Human Mammals

A detailed review of the toxicity of halogenated hydrocarbons has been published by von Oettingen (1964). Very little acute toxicity information on the monohalomethanes has been published since then, and no information is available for fluoromethane. Selected studies from von Oettingen's (1964) review and articles that have appeared in recent years are summarized in the following sections.

a. Acute Toxicity

In general, the symptoms produced by monohalomethanes are similar and suggestive of central nervous system involvement and of alterations in metabolism of glutathione and other sulfhydryl compounds. Because monohalomethanes are volatile, inhalation is the route of exposure studied most. Limited studies on other routes of administration (oral and subcutaneous) indicate that, regardless of route of administration, iodomethane would be classified as a toxic chemical under the Federal Hazardous Substances Labeling Act (Federal Register, 1962e). The relationship between the lethal doses resulting from inhalation and from oral doses is hard to assess in these studies, as the amount absorbed and the first-pass detoxification factor of the liver have not been determined. Based on the results of inhalation studies summarized below, bromomethane and chloromethane would also be classifed as toxic substances (LD_{50} of 200 to 20,000 ppm in 14 days in rats following one hour exposure).

Bromomethane

Lethal exposures to bromomethane occur in dogs exposed to 873.8 ppm for 30 to 40 minutes; in cats exposed to 17,990 ppm for 25 minutes; and in rabbits exposed to 218.45 ppm for 32 hours (von Oettingen, 1964).

Studies by Sayers et al. in 1929 (cited in von Oettingen, 1964) on guinea pigs are presented in Table 32. With the higher concentrations, the lungs were generally congested and edematous. The heart was frequently dilated, and at lower concentrations and with delayed deaths, dilation of the heart and degenerative changes in the heart muscle, liver, kidney, and occasionally in the pancreas were evident.

In a study of the acute toxicity of bromomethane inhalation in rats, Irish et al. (1940) found that prolonged exposures for up to 26 hours at a low concentration (218.5 ppm) were fatal (see Table 33 for details).

Gorbachev et al. (1962) found that rabbits died in 12 hours at an exposure of 591.1 ppm. They studied the metabolic effects of this dosage and a sublethal dosage which is detailed in Section III-B-2-c, p. 137. Balander and Polyak (1962) reported the LC_{50} in mice to be 395.8 ppm. Regardless of the experimental animal employed, death from bromomethane always seemed to involve marked changes in the central nervous system which were expressed in a variety of ways, including unsteady gait, twitchings, convulsions, and coma. Additionally, lung, liver, heart, and kidney changes were usually apparent.

Chloromethane

Mice exposed to chloromethane at 500 ppm for six hours daily for one week developed convulsions and usually died of terminal hemoglobinuria. Those animals which survived a 15-week exposure as outlined above developed a permanent tonic contraction of the adductor muscles in the hind and fore limbs. Guinea pigs succumb to 2,000 ppm during the second or third six-hour exposure, while dogs show symptoms of poisoning following a single six-hour exposure at 500 ppm and die following two to six exposures at 1,000 ppm or higher (von Oettingen, 1964).

Table 32. Effect of Various Concentrations of Bromomethane on Guinea Pigs*

Concentration (ppm)	Duration of Exposure (min)	Symptoms
50,000-96,000	7-15	Immediate uneasiness, after 1 to 2 min helpless on their side, struggling, convulsive respiration, death in 7 to 15 min
29,000	5	Fatal with 5 min exposure
22,000	30	Coughing in 7 min, retching, unsteadiness after 8 to 15 min, marked weakness after 30 min, death 10 min after exposure
13,000	43-68	Increased respiration after 13 min, inactivity, lacrimation, discharge from nose, weakness and unsteadiness in 23 to 28 min, convulsive respiration, death after 43 to 68 min
7,000	30 and 90	Effects similar to 13,000 ppm but delayed; exposure for 30 min fatal in 1-2 h, that for 90 min immediately
5,400	10 and 20	With 10 min exposure no apparent effect, with 20 min exposure no immediate effects, but death after 6 days
2,000-2,300	30	No symptoms, 1 of 6 animals died about 9 h after exposure
	90	Slight weakness, lacrimation and secretion about nose and mouth, later toleration of side position, death in 2-1/2 h or less
	170	All animals were dead at end of exposure
500-600	90	No fatalities
	270	Slight salivation and nasal discharge, all animals died during following 2 days
	440	3 out of 6 animals dead at end of exposure
	480	All animals died within 3-1/2 h after exposure

* Sayers _et al_., 1929, cited by von Oettingen, 1964

Table 32. Effect of Various Concentrations of Bromomethane on Guinea Pigs (Cont'd)

Concentration (ppm)	Duration of Exposure (min)	Symptoms
300	270	No symptoms and no deaths
	300	No symptoms during exposure, 1 of 6 animals died after exposure
	540	No symptoms during exposure
	810	All animals died 3 days following exposure
150	540	No symptoms during exposure, most animals died in 1-3 days
100	300 and 600	No symptoms and no fatalities

Table 33. Acute Toxicity of Methyl Bromide for Rats[*]

Concentration (ppm)	100% Fatality	100% Survival
12,850	10 mins	3 mins
5,140	24 mins	6 mins
2,570	42 mins	24 mins
514	6 hrs	2 hrs
257	22 hrs	8 hrs
218.5	26 hrs	12 hrs
107.9	---	22 hrs

[*] Irish *et al.*, 1940

Monkeys are convulsive following four to seven six-hour exposures to chloromethane at 2,000 ppm. Rats exposed for six hours daily to 3,000 and 4,000 ppm died one or two days after the third to fifth exposure, with severe spasmodic dyspnea, but without showing signs of the muscular spasticity described in other animals. Rabbits respond similarly following daily exposures to 2,000 or 4,000 ppm. Cats exposed daily for 6 hours to 2,000 ppm chloromethane became very weak after a week of exposure and were unable to right themselves. Continued exposure resulted in dyspneic respiration and a refusal to eat and drink. Death occurred after three to four weeks (von Oettingen, 1964).

It is apparent that chloromethane produces severe neurological disturbances in the animals tested. However, it appears less toxic than bromomethane; i.e., a six-hour exposure at 300 ppm bromomethane is lethal to guinea pigs, whereas two or three six-hour exposures at 2,000 ppm chloromethane are required to kill guinea pigs. Similar differences are noted in rats, cats, and dogs.

Iodomethane

Iodomethane causes death in mice after 10 minutes at exposure levels of 78,178 ppm. At exposures of 7,336 ppm, death ensues in one hour, even if exposed for only 30 minutes. At exposures between 3,668 and 5,373 ppm, death occurs within 2 to 2 1/2 hours, and continuous exposure at 72 to 723 ppm causes death within 24 hours. The LC_{50} in mice was determined to be 861 ppm for a 57-minute exposure. The oral LD_{50} for iodomethane suspended in arachis oil is 150 to 222 mg/kg in rats. Inhalation of iodomethane at 3,790 ppm for 15 minutes is lethal to rats within 11 days of exposure (von Oettingen, 1964). Animals lethally exposed showed severe neurological changes, as did those exposed to bromomethane and chloromethane.

In general, iodomethane appears to be the most toxic of the three monohalomethanes for which there is information. Taking the comparison in mice, iodomethane is lethal at 72 ppm in 24 hours; bromomethane is lethal within 2 to 3 days at 150 ppm following a nine-hour exposure; and chloromethane is lethal to 50% of the mice at 3,146 ppm following a six-hour exposure.

b. Subacute Toxicity

Bromomethane

There are little data available concerning subacute exposures of laboratory animals to bromomethane. However, Rosenblum et al. (1960) have indicated that dogs fed for one year with a bromomethane-fumigated diet (150 mg/kg/day residual bromide) were adversely affected. Actual bromomethane levels in the diet were not determined. When animals received a diet containing comparable amounts of sodium bromide (78 mg/kg/day residual bromide), no effects were noted. These results reenforce previous conclusions that bromomethane toxicity is not mediated by the level of bromide, but rather is determined by the extent of methylation of cellular macromolecules.

Feeding rats on wheat grain or peanuts fumigated with bromomethane and having residual bromide levels of 20 and 22 to 46 mg/kg, respectively, had no effect on weight gain (Vitte et al., 1970). No changes were detected in hemoglobin content or in red and white blood cell numbers. Likewise, Rosenblum et al. (1960) found no significant effects on hemoglobin, hematocrit, white or red blood cell counts, serum proteins, or blood urea nitrogen. Vitte et al. (1970) did detect changes in the iodine and calcium levels in the blood with pathomorphological changes in the thyroid and parathyroid glands. Vitte et al. (1970) also fed cats fumigated peanuts at 0.5 to 1.25 mg bromide/day for four months and observed no changes in motor response. Balander and Polyak (1962) have observed changes in motor responses within 40 minutes with an 18 ppm exposure of bromomethane.

Chloromethane

In a study on the constituents of cigarette smoke which were significant contributors to the change of mucus flow in cats, Weissbecker *et al.* (1971) isolated nine factors, one of which was chloromethane. Chloromethane caused an increase in mucus flow, and when added as a gas to a puff of cigarette smoke, diminished the mucostatic effect of other gases in the smoke, such as nitrogen oxide, nitrogen dioxide, and isoprene.

Chloromethane also has an effect on the circulatory and respiratory systems. Von Oettingen (1964) indicated that dogs exposed to concentrations of 15,000 and 40,000 ppm experienced increases in both respiratory and cardiac rates and in arterial and venous pressure within five minutes after exposure began. At the higher concentrations, this response was later followed by a depression in respiration, slowing of the heart rate, and a fall in the blood pressure. During the last phase of poisoning, there is sometimes a suggestion of changes in T-wave directions recorded in electrocardiograms.

Other subacute effects of chloromethane poisoning include restlessness in cats following a 10-minute exposure to either 30,840 or 87,380 ppm. Rabbits exposed to 4,883 and 2,570 ppm for 25 minutes experienced a depression in respiration but no death. Increases in exposure (8,147 ppm) brought about an increasing prevalence of neurological changes; i.e., irritation, restlessness, and convulsions. Some animals which survived a 20-hour exposure to 257 ppm later became paralyzed (von Oettingen, 1964).

Iodomethane

Exposures of 53 ppm and less iodomethane were not fatal in mice; however, these animals seemed depressed (von Oettingen, 1964). To compare the effects of iodomethane and the individual constituents of the chemical, Chambers *et al*., 1950 (cited in von Oettingen, 1964), decomposed iodomethane at 800°C and exposed rats to 60,550 ppm for 15 minutes. The animals that died upon removal from the chamber were autopsied and showed severe congestion of the trachea, lungs, liver, kidneys, and esophagus. There was severe erosion of the mucosa of the trachea and lungs, massive pulmonary hemorrhages, and edema. This indicates that the pyrolysis of iodomethane resulted in the formation of highly irritant and corrosive vapors. However, the fact that some animals survived for 14 days (LC_{100} for iodomethane in 15 minutes in rats is approximately 3,790 ppm) and showed no significant changes or neurological symptoms, would appear to indicate that these specific symptoms are the result of iodomethane exposure itself and not its decomposition products.

c. Repeated Doses and Chronic Studies

(i) Repeated Doses

Rats were exposed to repeated bromomethane doses of 108 ppm for 7-8 hours daily. Nine of the 30 rats exposed showed immediate loss of weight, nine were moribund after the ninth exposure, and two developed convulsions. Sixteen of the 30 animals appeared to tolerate 16 to 58 exposures fairly well, but five of these finally developed convulsions (Irish *et al*., 1940). Sokolova (1972) found that mice exposed twice to bromomethane in ship cargo areas for 18 hours at three-month intervals demonstrated alterations in conditioned reflex activity at 0.5 g/m^3, but not at 0.1 g/m^3.

These limited studies on protracted subacute exposures seem to indicate that the animals develop the same neurological responses as do those that were acutely exposed. This was also demonstrated in humans by Drawneek (1964) (see Section III-B-1).

(ii) Chronic Studies

As indicated in Section III-B-2-a, guinea pigs are not affected by a 10-hour exposure to 100 ppm bromomethane (Sayers _et al._, 1929, cited by von Oettingen, 1964), and rats survived 22 hours of exposure at 107.9 ppm (Irish _et al._, 1940). In a study on rabbits exposed by inhalation eight hours daily, five days a week for periods of six months or more, Irish _et al._ (1941) found that 22 days of exposure at 65 ppm (equivalent to 0.03 g/kg/day) produced the typical poisoning responses. Even at 33 ppm, irritation of the lungs and paralysis eventually occurred in rabbits, but not in rats, guinea pigs, or monkeys. At 16 ppm, bromomethane was tolerated by all species examined.

Smith and von Oettingen (1947 a) exposed (6 hours daily, 6 days weekly) ten different species to chloromethane at concentrations ranging from 300 to 4,000 ppm. At 2,000 ppm, mice, guinea pigs, and goats showed approximately equal susceptibility. At the same concentration (2,000 ppm), dogs were slightly more resistant, surviving 3 to 4 exposures with death occurring between the first and third exposure, and rabbits and rats were decidedly more resistant, dying after the fifth or sixth exposure. At 500 ppm, however, dogs showed the least resistance (surviving 2 weeks) and rabbits were less resistant than rats. Monkeys exposed to 2,000 and 500 ppm died within the same time ranges as did dogs.

On the exposure schedule which Smith and von Oettingen (1947 a) used (6 hours daily, 6 days weekly), mortality in rats was consistent with the product of time and concentration at exposure levels of 4,000 and 3,000 ppm. The same is true for rabbits (4,000 and 2,000 ppm), mice (3,000 and 2,000 ppm), and dogs and guinea pigs (3,000, 2,000, and 1,000 ppm). However, as the concentration decreased to 500 ppm, or with younger animals, the effects tended to accumulate more gradually. With concentrations of 300 ppm chloromethane for periods of up to 64 weeks, there was no evidence of cumulative toxicity, as all species survived. There were no behavioral or prolonged neurological studies performed on these animals that would give an indication of subtle neuropathological changes.

The high degree of susceptibility of dogs and monkeys to chloromethane at concentrations of 500 ppm is an important observation since this level is close to the TLV of 100 ppm. Among four dogs exposed, one died after two weeks, one after three weeks, and one after four weeks. All displayed symptoms identical to dogs poisoned at higher concentrations. The fourth dog survived 29 weeks of exposure but developed irreversible neuromuscular damage. The two treated monkeys died as a result of 16 and 17 weeks of exposure, respectively, after suffering progressive debility and terminal persisting unconsciousness. From the work of Smith and von Oettingen (1947 a), there appears to be a range between 300 and 500 ppm where overt symptoms of chloromethane poisoning are first detectable in dogs and monkeys. However, detailed neurological and behavioral analyses of these animals exposed to low concentrations were not undertaken.

In summary, chronic chloromethane exposures of greater than 300 ppm are not tolerated well in the species examined. Chronic bromomethane exposures as low as 33 ppm have been demonstrated to cause lung damage in rabbits. During chronic bromomethane exposures to 65 ppm, monkeys were adversely affected, and at chronic exposures to 108 ppm, death resulted within three weeks in rats, guinea pigs, rabbits, and monkeys. No chronic studies on iodomethane exposure were found in the literature.

d. Absorption, Distribution, and Excretion

In a recent study, Williford et al. (1974) exposed rats to bromomethane-fumigated diets with 290, 600, and 1,177 ppm residual bromide. Results showed the eye to have the highest concentration of residual bromide of all tissue analyzed. Table 34 shows the results obtained when animals were exposed to the diets for 56 days. In a second experiment at 1,177 ppm, rats were sacrificed every two weeks, and the results are presented in Table 35. The rapid uptake of bromide in the eye occurred between days 14 and 42, with a 60% reduction between days 42 and 56. The muscles had low levels of bromide when compared with other tissues, as did abdominal fat (Table 35); however, the levels in various muscles and organs in group 4 (1,177 ppm) exceed the permissible (125 ppm) levels of bromide allowed by the FDA (CFR, 1972). The results presented in this study would seem to indicate that further study is needed on the effects of bromomethane in organs where accumulation occurs.

Since it is a gas at temperatures above 35°C, bromomethane is usually encountered as a vapor; accordingly absorption and excretion commonly occur in the lungs. Some absorption, particularly when bromomethane is present as a liquid, can occur through the skin (von Oettingen, 1964). Increases in plasma bromide levels in all species tested indicate a rapid uptake of bromomethane or its metabolites. However, its toxic effects do not seem to be dependent on a specific plasma level of bromide. The earlier postulates of methanol and bromine being the toxins no longer seem valid.

Table 34. Mean Bromide Content (ppm) of Certain Organs and Tissues of Rats Fed Diets Containing Bromide[a], *

Tissue	Control (12)[b]	Diet 290 ppm (10)	600 ppm (11)	1177 ppm (12)
Blood	11.4	208.8	372.3	631.1
Lungs	15.7	218.6	416.2	648.2
Spleen	11.9	179.9	319.1	541.3
Kidneys	10.9	139.3	292.1	527.9
Heart	14.8	106.5	211.9	359.7
Liver	6.2	91.4	175.9	304.5
Eye	16.1	251.0	492.4	856.8
Testes	12.9	176.7	333.0	610.6
Bone	14.3	82.3	164.6	383.8
Triceps	8.2	59.6	108.5	178.8
Gastrocnemius	5.8	52.0	103.1	179.5
Fat	2.5	26.8	57.2	99.3

[a] All treatment means significantly different at $P < .01$.

[b] Numbers in ( ) are number of animals in each group.

*Williford et al., 1974

Table 35. Bromide Content of Blood, Certain Organs and Tissues of Rats[b]

		Means of Bromide Levels									
Group	Days on Diet	Blood	Lung	Spleen	Kidney	Liver	Heart	Eyes	Testes	Triceps	Gastrocnemius
1	14	712.8	675.9	662.1	502.0	332.2	424.2	1531.1	501.7	318.2	234.9
2	28	671.5	748.3	683.4	556.7*	307.5	423.1	2252.6	558.3	327.8	318.7**
3	42	620.1	697.0	662.5	470.4	299.1	356.0	2154.4	571.2	259.7	238.7
4	56	663.7	664.8	518.8	470.1	292.8	355.7	850.0*	496.2	216.0	182.3**

[a] All animals in each group were fed the 1177 ppm diet.

*Mean significantly different from other three treatment means at $P < .05$.

**Mean is significantly different from group four treatment mean at $P < .01$.

[b] Williford *et al.*, 1974

Irish et al. (1941) showed that it is very unlikely that the formation of methanol may be responsible for the toxic action of bromomethane. Further, their results indicated that the toxicological characteristics of bromomethane were not due to bromide. Specifically, Irish et al. (1941) exposed rats to bromomethane by either single doses for 3 minutes to 32 hours, or repeatedly for 7 1/2 to 8 hours/day, 5 days/week, for at least 6 months. Some of the bromomethane that was absorbed was broken down in the body as indicated by a rise in the bromide level in the blood. Normal bromide level in rabbits is 1 mg/100 ml. In the multiple dose experiments using 60 ppm bromomethane, the blood bromide rose to 11 mg/100 ml. Feeding inorganic bromide in amounts sufficient to maintain blood bromide above this level (62 mg/100 ml) failed to produce a comparable functional response. Likewise, rabbits exposed to concentrations of methanol vapor equivalent to or greater than that which would be obtained by the hydrolysis of intoxicating concentrations of bromomethane failed to show any functional response comparable to that of animals exposed to bromomethane. Even rabbits given 20 exposures to 5,000 ppm methanol and 0.1 gm/kg oral doses of sodium bromide failed to show any functional responses comparable to bromomethane intoxication, even with blood bromide levels of 90 mg/100 ml. Bromomethane ingestion in olive oil gave the same response as bromomethane inhaled. These authors felt that these results strongly indicate the probability that the functional response in animals is due to the alkyl halide molecule and its reaction with the tissue (e.g., methylation of critical cellular proteins).

Lynn et al. (1963) found that bromide is secreted in the milk of lactating cows when fed forage or grain treated with bromomethane or sodium bromide. A larger fraction of ingested bromide was secreted in the milk when bromomethane, rather than sodium bromide, was fed (see Table 36). This suggests that inorganic bromides are more poorly absorbed or excreted by different routes than bromomethane. There appears to be a time (20 to 30 days) after which the bromide levels in the milk reach a steady state concentration, indicating a balance between absorption and excretion mechanisms.

Lane and coworkers (1969) fed bromomethane-fumigated diets to cows, calves, and piglets for 90 days. They observed an initial rise in bromide levels in the blood which soon reached a steady state. They concluded that the bromide concentrations in milk and organs did not constitute a human hazard.

From these studies it appears that bromide levels increase in blood, milk, and tissues of animals fed bromomethane-treated feed. However, these levels return to normal when the feed is removed (Lane et al., 1969).

Chloromethane boils at -23.7°C and is therefore generally encountered as a gas. It is readily absorbed through the lungs and somewhat by the skin. It reaches only moderate levels in the blood, even under continuous exposure conditions. Following an intravenous injection of chloromethane (conditions unspecified), 80% is lost almost immediately, with less than 10% remaining an hour after injection (von Oettingen, 1964). During the first hour, 5% is excreted via the bile and urine and 5% via the lungs. The fate of the rest is speculative, but chloromethane is probably sequestered much as is bromomethane by sulfhydryl groups present in various proteins and enzymes.

Table 36. Relationship between Bromide Ingestion and Bromide Levels in the Milk of Cows*

Feed	PPM Bromide	Bromide Ingested per Day (mg)	Milk Produced per Day (kg)	PPM Bromide in Milk	Bromide Secreted in Milk per Day (mg)	Ratio of Bromide Secreted in Milk to Bromide Ingestion
Grain (CH_3Br-treated)	53	185	13.7	8	109	0.59
	100	350	13.2	8	106	0.30 Av. 0.38
	220	770	13.2	15	198	0.26
Grain (NaBr-treated)	50	175	13.2	2	26	0.15
	100	350	13.2	4	53	0.15 Av. 0.18
	200	700	13.2	12	159	0.23

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*Modified from Lynn et al., 1963

Reynolds and Yee (1967) found that the patterns of ^{14}C incorporation *in vivo* from CCl_4, $CHCl_3$, CH_2Cl_2, and CH_3Cl into the chemical components of subcellular fractions of liver were distinctive for each of the four chloromethanes. The relative amounts of nonvolatile ^{14}C recovered in lipids and in microsomes at two hours after oral administration (830 or 2600 μm/100 g body weight) increased with increasing chloromethane chlorine content, whereas that recovered in proteins, acid-soluble constituents, and cell sap decreased. Protein-bound ^{14}C following these chloromethane exposures occurred at an amino acid locus corresponding to serine. Formaldehyde-^{14}C was also found to label serine. This labelling of serine by formaldehyde-^{14}C is interesting in light of the results reported by Evtushenko (1966) that in rabbits exposed to chloromethane (route unspecified), plasma levels of formaldehyde ranged from 0.65 to 1.32 ng/100 ml.

There is an increased excretion of urinary or fecal coproporphyrin III following chloromethane exposure (Chalmers *et al*., 1940). Glutathione (GSH) accelerates the transfer of iron to protoporphyrin, and the loss of GSH by methylation (see Section III-B-2-e, p. 147, for details of metabolic aberrations) may reduce the rate of heme formation. The excretion of coproporphyrin III may represent the excretion of protoporphyrin by an alternative pathway (Redford-Ellis and Gowenlock, 1971 b).

Barnsley and Young (1965) studied the fate of iodomethane by injecting 50 mg/kg subcutaneously in rats and studying the urinary excretions. S-Methylcysteine, methylmercapturic acid, methylthioacetic acid, and N-(methyl-thioacetyl)glycine were all isolated. Barnsley and Young (1965) have proposed a scheme for the metabolism of iodomethane which is presented in Section III-B-2-e.

While iodomethane is the only halomethane which is usually in the liquid state (boils at 42.5°C), it can also be absorbed via the lungs as well as by the gastrointestinal tract. Information on its fate and distribution in the organism is limited. In addition to the results described by Barnsley and Young (1965) above, Jaquet (1901, cited by von Oettingen, 1964) stated that larger quantities of iodomethane may be detected in the urine 12 days after exposure.

e. Metabolic Effects

Mizyukova and Bakhishev (1971) found that when cysteine was given orally or subcutaneously 30 minutes before or within 5 minutes after acute lethal bromomethane poisoning in rats, mice, and rabbits, it proved to be an effective therapeutic agent. Cysteine restored the level of sulfhydryl groups and prevented changes in carboxyl and amino groups in whole blood, serum, and protein and nonprotein fractions. Cysteine prevented death, paralysis, paresis, and spasms which developed on the third and fourth days after bromomethane inhalation in untreated animals.

In rabbits exposed to a threshold concentration of 25 ppm bromomethane for 4.5 months, Balander and Polyak (1962) observed changes in several oxidative-reduction reactions in the neuro-endocrine regulations of metabolism. Gorbachev _et al_. (1962), in acute inhalation studies in rabbits, observed increased oxygen demand in the brain and decreased cellular respiration in the kidney. In a four month chronic study (conditions not specified), rabbits developed hypoglycemia. In another study on rabbits, Kakizaki (1967) exposed animals from 20 to 120 mg/kg bromomethane in olive oil by subcutaneous injection. Toxicologic responses were paralysis of hind limbs, cessation of drinking, and a reduction in urine output. Levels above 50 mg/kg resulted in a sharp elevation of free bromide in the blood and reductions of platelet count, blood serotonin, and blood water.

Redford-Ellis and Gowenlock (1971 a, b) have extensively studied the effects of chloromethane on rat and guinea pig brain, liver, and kidney homogenates. The uptake of chloromethane by these three tissues exposed to 520 to 790 μg/g wet tissue was: brain, 100 μg/hr/g wet tissue; liver, 160 μg/hr/g wet tissue; and kidney, 20 μg/hr/g wet tissue. In the liver, ^{14}C-S-methylglutathione (GSMe) and ^{14}C-S-methylcysteine (S-MeCys) were formed directly from the labelled substrate. In the kidney and brain, ^{14}C-SMeCys and ^{14}C-GSMe were formed, and methylation of cysteine SH-groups was demonstrated in the mixed insoluble proteins. In the kidney, protein traces of labelled methionine were found. The brain and kidney homogenates hydrolyzed ^{14}C-GSMe. No effect on the thiol-dependent enzymes succinate dehydrogenase or yeast alcohol dehydrogenase could be demonstrated, even with 23 hours exposure. Exposure of 200 mg brain to 1,970 μg chloromethane had no effect on oxygen uptake during a three and one-half hour exposure. These authors suggested that the intracellular accumulation of GSMe might account for some of the clinical features of intoxication.

Nozdrachev (1974), in studies on acute (LD_{50}) and chronic (1/200 LD_{50}) poisoning with chloromethane (conditions unspecified), found elevated aldolase activity in tissues and blood serum. Phosphoglucomutase activity declined in both the acute and chronic poisonings. Administration of cysteine prevented death in those animals acutely poisoned.

From the above observations, the following biochemical and metabolic actions of chloromethane may be suggested.

The reaction of chloromethane with GSH not only removes GSH, but also produces GSMe, which is an intracellular inhibitor of GSH. Since it has been shown that glutathione conjugates of alkylating agents are excreted in the bile (Boyland et al., 1961), high levels of GSMe should not accumulate in the liver of the intact animal. The kidney, likewise, is able to hydrolyze GSMe and excrete S-MeCys (Barnsley, 1964). It appears likely, therefore, that adequate amounts of cysteine, either free or in combination with glutathione or protein, are essential for the detoxification of chloromethane in mammalian systems. A similar mechanism probably exists for all of the monohalomethanes.

The physiological role of GSH is uncertain, although it has several hard-to-assess specific coenzyme functions. Few biochemical changes have been described in organisms poisoned by monohalomethanes, and their relationship to these findings needs to be considered. GSH acts as a cofactor in the glyoxalase system which catalyzes the conversion of methylglyoxal to lactic acid, while GSMe inhibits this enzyme (Kermach and Matheson, 1957, cited by Redford-Ellis and Gowenlock, 1971 b). The symptoms of monohalomethane intoxication are similar to those seen in cats following intoxication by methylglyoxal; i.e., convulsions, initial excitement followed by listlessness, anuria, anorexia, coma, and death. Redford-Ellis and Gowenlock (1971 b) conclude that death from chloromethane intoxication may be by the accumulation of methylglyoxal in the brain.

Using bromosulphalein retention as an indicator of liver damage and metabolic alteration, Kutob and Plaa (1962 a) compared this procedure to the standard histologic evaluations in mice given subcutaneous injections of either 0.2 or 0.8 mM/kg iodomethane. No response was observed at the 0.2 mM/kg concentration; however, at 0.8 mM/kg the bromosulphalein retention indicated liver damage in 30% of the exposed animals, while the histopathological evaluation indicated that 40% were affected. In further studies Kutob and Plaa (1962 b) developed a screening procedure for estimating hepatotoxic potential of industrial solvents in mice given by subcutaneous injection. Data on lethality, barbiturate sleeping time, and bromosulphalein retention, coupled with minimal histologic examination, were employed for nine halogenated methane derivatives. Six of the nine were found to be hepatotoxic using three parameters. None of the dihalogenated compounds were hepatotoxic. Iodomethane had a relative potency of 70 when carbon tetrachloride was assigned a value of 100. Only carbon tetrachloride and carbon tetrabromide (220) had potencies higher than iodomethane. Triiodomethane, trichloromethane, and tribromomethane all had lower relative potencies (30, 10, and 8, respectively).

After the subcutaneous injection of iodomethane (50 mg/kg) to male rats, S-methylcysteine, methylthioacetic acid, methylmercapturic acid and N-(methylthioacetyl)glycine were recovered (Barnsley and Young, 1965). One pathway for the formation of these various compounds probably involves the formation of S-methylglutathione (V) as an intermediate. Other workers (Redford-Ellis and Gowenlock, 1971 a, b; Boyland et al., 1961; Barnsley, 1964) have shown that the liver contains enzymes which catalyze the reaction of alkyl halides with glutathione. Moreover, the metabolism of S-methylglutathione gives rise to a number of metabolites which have been isolated following the injection of iodomethane (Foxwell and Young, 1964, cited in Barnsley and Young, 1965). The scheme of iodomethane metabolism as outlined by Barnsley and Young (1965) is presented in Figure 14.

Johnson (1966) has found that iodomethane is converted to S-methylglutathione in the liver and excreted in the bile. The conjugation

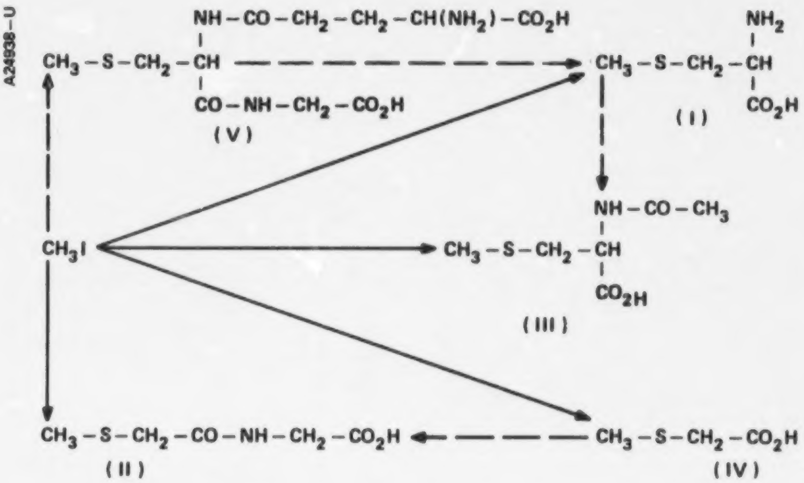
A24938-U
NH–CO–CH2–CH2–CH(NH2)–CO2H
CH3–S–CH2–CH
CO–NH–CH2–CO2H
(V)
NH2
CH3–S–CH2–CH
CO2H
(I)
NH–CO–CH3
CH3I
CH3–S–CH2–CH
CO2H
(III)
CH3–S–CH2–CO–NH–CH2–CO2H
(II)
CH3–S–CH2–CO2H
(IV)

Figure 14. Scheme of Iodomethane Metabolism (Conversions demonstrated by Barnsley and Young (1965) are shown in continuous lines, and possible metabolic pathways are shown by broken lines.)

process was reproduced in vitro and found to be enzymatically catalyzed. In kidney homogenates, S-methylglutathione was degraded to S-methylcysteine and was excreted as compounds related to methylmercapturic acid, thus adding further support to the work of Barnsley and Young (1965).

Hasegawa et al. (1971) attempted to determine a means for early diagnosis of iodomethane and bromomethane poisoning by observing changes in blood lipid levels. This work was carried out on rabbits receiving a subcutaneous injection of 53.5 to 57.0 mg/kg iodomethane. The most striking change observed was a significant increase in serum triglycerides (Table 37). The change was more remarkable in the blood than in the brain. These findings in animals were further substantiated by the examination of men exposed to iodomethane or bromomethane. Serum lipid content (especially triglyceride content) in poisoned men who had no self-consciousness of nervous disorder showed a fairly sharp increase.

In summary, the monohalomethanes cause a variety of metabolic dysfunctions. Decreases in aldolase activity in the Kreb Cycle and amounts of GSH in the liver, brain, and kidney result from exposure. Increases in methylglyoxal in the brain due to aberrations in GSH metabolism may prove to be one of the causative agents in the neurological damage seen in monohalomethane poisoning. Increases in serum lipid content which appear prior to any physiological or neurological changes in subjects exposed to monohalomethanes should be further analyzed. Studies with a large cohort of occupationally-exposed workers would help determine the utility of this parameter as a possible screening technique for subacute exposure to monohalomethanes.

Table 37. Effect of Methyl Iodide on Serum Lipid

No. of rabbits	10			11			12			13			14		
Lipid fraction	0 (hr)	48 (hr)	P (%)	0 (hr)	48 (hr)	P (%)	0 (hr)	48 (hr)	P (%)	0 (hr)	48 (hr)	P (%)	0 (hr)	48 (hr)	P (%)
Phospholipid	81.8	135.0	165	73.4	118.0	161	47.3	103.5	219	92.5	76.5	83	66.0	119.6	181
Cholesterol	23.6	42.8	181	23.6	40.7	172	11.5	33.0	277	21.7	29.7	137	16.0	49.9	312
Free fatty acid	32.2	91.0	283		8.8		2.5	5.9	236	12.7	18.1	143	4.8	28.6	596
Triglyceride	33.8	31.2	101.0	50.9	126.4	248	19.0	117.6	619	38.7	53.6	139	27.3	222.8	816
Estercholesterol	75.8	64.8	86	68.0	79.5	117	29.9	69.1	231	59.9	116.8	195	37.1	78.3	211
Total lipids	247.2	675.6	274		373.4		110.2	329.1	299	225.5	294.7	131	151.2	499.2	330

P: % of increase. Rabbits were injected with 57 mg of methyl iodide per kg of body weight. The amount of lipid determined before and after 48 hours of the injection was represented as mg per dl of serum.

* Hasegawa _et_ _al_., 1971

f. Teratogenicity/Mutagenicity/Carcinogenicity

No reports of teratogenicity have been published on any of the monohalomethanes. In part, this may be due to the fact that in the past only men were employed in the application of pesticides, in the manufacture and maintenance of fire extinguishers, and in the refrigerant coolant industry. However, the possibility that women of child-bearing age may be exposed to any of these monohalomethanes would seem to necessitate the need for appropriate teratogenic data. Reports of altered enzymatic functions in adults and of neuroendocrine changes, as well as the effect on sulfhydrylic compounds, could have profound effects on the developing nervous and endocrine systems of a fetus. Indeed the work by Williford _et al_. (1974), where large increases in bromide levels were found in the eye and testes following the consumption of bromomethane-fumigated food, could have teratogenic implications. While no report of teratogenicity has been found, the need for a screening of the monohalomethanes for teratogenic effects seems to be indicated.

Iodomethane has been reported by several researchers to cause carcinogenic activity in rodents and is implicated as a carcinogen in the standard Ames test. Gribble (1974) reported that 50 mg/kg in single or 10 mg/kg weekly subcutaneous injections produced massive local sarcomas in rats. This is well below the LD_{50} of 110 mg/kg. However, when iodomethane was administered intravenously or orally, no sarcoma development was observed. The author pointed out that similar results have been obtained with other substances such as benzyl chloride. Using the Salmonella/microsome test, McCann _et al_. (1975) have classified iodomethane as a limited carcinogen; i.e., a weak mutagen.

In mice injected weekly for 24 weeks with a total dose of 0.31 mmoles/kg of iodomethane, Poirier _et al_. (1975) reported an increase in lung adenomas. Eleven of twenty experimental animals survived the treatment, and five of these had lung tumors. Of the 17 alkyl halides tested, on a molar dose basis, iodomethane was the most active compound.

Andrews et al. (1976) have tested chloromethane at various concentrations using the Ames test. The *Salmonella typhimurium* tester strain TA1535 was used, and the mean values for the number of revertant colonies at the various concentrations are indicated in Table 38. With the exception of 0.5%, all levels were significantly different ($p < 0.01$) when compared to non-gassed controls. A level of 23% chloromethane was toxic to bacteria. The addition of rat liver homogenate (S9) is not required to detect mutagenesis, implying that bioactivation is not essential.

Studies implicating bromomethane as either a carcinogen or mutagen were not found. From the above information, the most active carcinogenic/mutagenic compound of the monohalomethanes for which there is information is iodomethane, followed by chloromethane and then, questionably, by bromomethane.

g. Behavioral Effects

Various workers have reported the spectrum of effects due to monohalomethane poisoning. Among these changes are neurological and psychological alterations which affect behavior.

Rabbits exposed to 53 ppm iodomethane appear depressed and less active than control animals (Bachem, 1927, cited in von Oettingen, 1964). While both iodomethane and bromomethane cause muscle spasticity in rabbits, chloromethane does not (von Oettingen, 1964). Chloromethane poisoning in other animals (dogs, cats, guinea pigs, and monkeys), however, does cause this muscular spasticity. The only animal in which no spasticity was noted was the rat (von Oettingen, 1964).

Table 38. Mutagenic Activity of Chloromethane Using Salmonella typhimurium Tester Strain TA1535[*]

Gas	Concentration (%)	Mean Values[a] ± SD for the Number of Revertant Colonies for Strain TA1535	
		S9 Absent	S9 Added
None	---	28.9 ± 6.24	14.9 ± 3.70
CH_3Cl	0.5	31.6 ± 5.55	46.6 ± 8.26
	0.8	53.6 ± 4.04	79.4 ± 9.71
	3.8	239.2 ± 43.79	268.8 ± 40.38
	8.7	928.0 ± 179.24	1046.4 ± 144.27
	13.3	1600.0 ± 329.46	1939.2 ± 558.56
	20.7	1558.4 ± 159.44	2038.4 ± 416.10

[a] Of five replicates.
[*] Modified from Andrews et al., 1976

Cats exposed to chloromethane (conditions unspecified) also refused to eat and drink, as did rabbits, and became quite weak with hyperactive tendon reflexes. Cats exposed to 30,840 ppm bromomethane became restless, and some became narcotized and later had uncontrolled salivation and became uncoordinated. Rabbits likewise salivate freely and become restless on exposure to bromomethane.

The monohalomethanes produce a diffuse stimulation of the central nervous system which is expressed first as restlessness, then by muscle twitching, and finally, tonic responses. Vegetative functions, such as eating, drinking, and righting, are also affected by the monohalomethanes. These effects first appear in rabbits at levels such as 53 ppm iodomethane, 257 ppm bromomethane, and 2,000 ppm chloromethane (von Oettingen, 1964).

3. Effects on Other Vertebrates Including Birds, Fish, Amphibians, and Reptiles

a. Fish and Reptiles

No information regarding monohalomethane exposure to fish or reptiles was found, even though iodomethane, bromomethane, and chloromethane have all been detected in marine waters.

b. Amphibians

Frogs tolerated exposure to 2,000 ppm chloromethane in the diet for 131 days and to 300 ppm for 448 days. Only one death out of six animals exposed to 2,000 ppm was observed, and this could be attributed to starvation rather than chloromethane exposure. In a group of frogs exposed to 300 ppm for 448 days, no deaths were recorded (Smith and von Oettingen, 1947 a).

c. Birds

Four chickens were exposed to 2,000 ppm chloromethane in the diet starting when they were 11 weeks old. After three weeks exposure, the legs became weak and abducted, and the chickens were unable to walk. Debility and paralysis increased until the entire body (except the neck and head) was paralyzed and cold to the touch. Death followed five to six weeks of exposure (Smith and von Oettingen, 1947 b).

Getzendaner (1965) found that the bromide content of eggs and chicken tissues reaches a maximum in 30 to 40 days when the dietary intake of bromomethane-fumigated feed is maintained at a fixed level. Laying hens were maintained on diets containing from 5 to 410 ppm of bromide residue. Eggs were collected over a period of 70 days and hens were sacrificed at 28, 44, 56, and 70 days. At equilibrium, ratios of average bromide residues in the tissues to the feed content were: whole eggs, 1.0; yolks, 1.2; whites, 0.8; egg shells, 0.3; light meat, 0.2; darkmeat, 0.3; skin, 0.4; liver, 0.5; feathers, 0.6; kidneys, 0.8; and blood, 1.7.

4. Effects on Invertebrates Including Annelids, Arthropods, and Crustaceans

a. Insects (Bromomethane and Iodomethane Only)

(i) Acute Toxicity

Table 39 summarizes information on the acute toxicity of bromomethane to various insects. An immense variety of insects can be controlled by bromomethane fumigation.

Iodomethane has also been used as a fumigant against the grainery weevil (Ferguson and Pirie, 1948), against the Oriental fruit fly (Burditt _et al_., 1963, and Balock, 1951), and the Mediterranean fruit fly (Burditt _et al_., 1963). Muthu and Srinath (1974) reported the toxicity of iodomethane to insects commonly found in processed and packaged food products. In a 24-hour saturation exposure of iodomethane, the following LD_{50}'s were determined: _Oryzaephilus surinamensis_, 2.0 mg/l; _Rhyzopertha dominica_, 1.2 mg/l; _Sitophilus oryzae_, 1.1 mg/l; _Stegobium paniceum_, 1.0 mg/l; and _Tribolium castaneum_, 2.6 mg/l. Iodomethane appears to be an effective fumigant against insects, but somewhat less toxic than bromomethane.

No information was available on the effects of chloromethane or fluoromethane on insects.

(ii) Metabolic Effects

Bond (1956, 1975), working with _Tenebroides mauritanicus_, noted the susceptibility of insects to bromomethane was correlated with the rate

Table 39. Insects Controlled by Bromomethane

Insect	Dosage	Conditions/Results	Source
Trogoderma granaria	9.7 ppm	LD_{50} larvae	Pradhan and Govindan, 1954
Tribolium castaneum	1.5 ppm	LD_{50} adults	
Tenebroides mauritanicus	23 mg/l	LD_{99}	Bond, 1956
	16 mg/l	LD_{50}	
	10 mg/l	Maximum sublethal dose	
Onychuirus hortensis	2 cc/ft^2	Bromomethane: chloropicrin (2:1), covered for 14 days - complete kill	Edwards, 1962
Tribolium confusum	3.60 mg/l	LD_{50} at 80°F, in 16 hrs	Kenaga, 1961
	9.57	in 5 hrs	
	22.68	in 2 hrs	
	4.64	LD_{95} at 80°F, in 16 hrs	
	11.84	in 5 hrs	
	27.90	in 2 hrs	
	5.05	LD_{50} at 60°F, in 16 hrs	
	17.24	in 5 hrs	
	41.28	in 2 hrs	
	5.80	LD_{95} at 60°F, in 16 hrs	
	23.21	in 5 hrs	
	55.02	in 2 hrs	
	6.64	LD_{50} at 40°F, in 16 hrs	
	26.71	in 5 hrs	
	90.75	in 2 hrs	
	13.08	LD_{95} at 40°F, in 16 hrs	
	37.93	in 5 hrs	
	145.14	in 2 hrs	
Araecerus fasciculatus	6.2 mg/l	LD_{95} for eggs in 6 hrs	Majumder *et al.*, 1961
	3.4	LD_{95} for larvae in 6 hrs	
	7.4	LD_{95} for pupae in 6 hrs	
	4.5	LD_{95} for adults in 6 hrs	

Table 39. Insects Controlled by Bromomethane (Cont'd)

Insect	Dosage	Conditions/Results	Source
Antagenus picus	2 lbs/ft^3	bromomethane with 0.5% chloropicrin provided control	Pence and Morganroth, 1962
Anthrenus verbasci	2 lbs/ft^3		
Anthrenus fluirpes	2 lbs/ft^3		
Plodia interpunctella	5.5 mg/1	LD_{50} normal larvae	Sardesai, 1972
	10.2 mg/1	LD_{50} diapausing larvae	
Anthonomus grandis	16 mg/1	100% mortality, 32°C, 1 hr	Roth and Kennedy, 1972
	16	100% mortality, 22°C, 2 hr	
	32	100% mortality, 16°C, 3 hr	
	32	100% mortality, 8°C, 3 hr	
	48	100% mortality, 6°C, 2.25 hr	
	80	100% mortality, 4°C, 5 hr	
	16	100% mortality, 1°C, 16 hr	
Tribolium confusum	15 mg/1	24 hrs preceded by 10-50 Krad	Cogburn and Gillenwater, 1972
Ephestia kuehniella	2.46 mg/1	5 hrs exposure 1 day old eggs provided control	Mostafa *et al.*, 1972
	2.28	5 hrs exposure 2 day old eggs provided control	
	2.15	5 hrs exposure 3 day old eggs provided control	
	2.24	6 hrs exposure 1 day old eggs provided control	
	2.13	6 hrs exposure 2 day old eggs provided control	
	2.05	6 hrs exposure 3 day old eggs provided control	
	2.20	7 hrs exposure 1 day old eggs provided control	
	2.08	7 hrs exposure 2 day old eggs provided control	
	2.02	7 hrs exposure 3 day old eggs provided control	

Table 39. Insects Controlled by Bromomethane (Cont'd)

Insect	Dosage	Conditions/Results	Source
Sitotroga cerealella	2.21 mg/1	5 hrs exposure 1 day old eggs provided control	Mostafa *et al.*, 1972
	2.13	5 hrs exposure 2 day old eggs provided control	
	1.98	5 hrs exposure 3 day old eggs provided control	
	2.14	6 hrs exposure 1 day old eggs provided control	
	1.93	6 hrs exposure 2 day old eggs provided control	
	1.87	6 hrs exposure 3 day old eggs provided control	
	1.94	7 hrs exposure 1 day old eggs provided control	
	1.91	7 hrs exposure 2 day old eggs provided control	
	1.85	7 hrs exposure 3 day old eggs provided control	
Tribolium castaneum	3.92 mg/1	5 hrs exposure 1 day old eggs provided control	Mostafa *et al.*, 1972
	3.65	5 hrs exposure 2 day old eggs provided control	
	3.38	5 hrs exposure 3 day old eggs provided control	
	3.42	6 hrs exposure 1 day old eggs provided control	
	3.27	6 hrs exposure 2 day old eggs provided control	
	3.06	6 hrs exposure 3 day old eggs provided control	
	6.19	7 hrs exposure 1 day old eggs provided control	
	6.02	7 hrs exposure 2 day old eggs provided control	
	5.85	7 hrs exposure 3 day old eggs provided control	
Sitophilus oryzae	6.19 mg/1	5 hrs exposure 1 day old eggs provided control	Mostafa *et al.*, 1972
	6.02	5 hrs exposure 2 day old eggs provided control	
	5.85	5 hrs exposure 3 day old eggs provided control	
	5.97	6 hrs exposure 1 day old eggs provided control	
	5.88	6 hrs exposure 2 day old eggs provided control	
	5.56	6 hrs exposure 3 day old eggs provided control	
	5.71	7 hrs exposure 1 day old eggs provided control	
	5.59	7 hrs exposure 2 day old eggs provided control	
	5.45	7 hrs exposure 3 day old eggs provided control	
Laspeyresia pomonella	32 g/m^3	2 hrs at 17°C provided control	Morgan *et al.*, 1974
Oryzaephilus mercator	0.2 g/1	1 hr at 24°C provided control	Joshi, 1974

Table 39. Insects Controlled by Bromomethane (Cont'd)

Insect	Dosage	Conditions /Results	Source
Corcyra cephalonica	1.775 mg/1	5 hr exposure 1 day old eggs provided control	El-Buzz et al., 1974
	1.660	5 hr exposure 3 day old eggs provided control	
	1.099	5 hr exposure 1st larval instar provided control	
	1.318	5 hr exposure 3rd larval instar provided control	
	1.680	5 hr exposure last larval instar provided control	
	2.790	5 hr exposure 3 day old pupae provided control	
Trogoderma variable	32 mg/1	2 hr exposure at 21.1°C, 1 day old eggs provided control	Vincent and Lindgren, 1975
	40	2 hr exposure at 21.1°C, 2 day old eggs provided control	
	32	2 hr exposure at 21.1°C, 3 day old eggs provided control	
	32	2 hr exposure at 21.1°C, 4 day old eggs provided control	
	32	2 hr exposure at 21.1°C, 5 day old eggs provided control	
	32	2 hr exposure at 21.1°C, 6 day old eggs provided control	
	32	2 hr exposure at 21.1°C, 7 day old eggs provided control	
	24	2 hr exposure at 21.1°C, 8 day old eggs provided control	
	24	2 hr exposure at 21.1°C, 2nd instar larvae provided control	
	40	2 hr exposure at 21.1°C, 5th or 6th instar larvae provided control	
	40	2 hr exposure at 21.1°C, pupae provided control	
	36	2 hr exposure at 21.1°C, adults provided control	
	36	2 hr exposure at 15.6°C, 2nd instar larvae provided control	
	56	2 hr exposure at 15.6°C, 5th or 6th instar larvae provided control	
	72	2 hr exposure at 15.6°C, pupae provided control	
	36	2 hr exposure at 15.6°C, adults provided control	
	16	2 hr exposure at 26.7°C, 2nd instar larvae provided control	
	32	2 hr exposure at 26.7°C, 5th or 6th instar larvae provided control	
	32	2 hr exposure at 26.7°C, pupae provided control	
	24	2 hr exposure at 26.7°C, adults provided control	
Gryllotalpa (mole crickets)	70-100 g/m^2	24 hr exposure provided control	Dzidzariya, 1972
Caterpillars	70-100 g/m^2	24 hr exposure provided control	
Agrolis (cutworms)	70-100 g/m^2	24 hr exposure provided control	
Tenebroides mauritanicus	43.3 mg/1	LD_{50} at 35 mm pressure	Monroe et al., 1966
	25.5 mg/1	LD_{50} at 100 mm pressure	
Tribolium confusum	23.7 mg/1	LD_{50} at 75 mm pressure	
	21.5 mg/1	LD_{50} at 100 mm pressure	

Table 39. Insects Controlled by Bromomethane (Cont'd)

Insect	Dosage	Conditions/Results	Source
Hemp leaf roller	40-45 g/m^3	18 hrs at 10-15°C and hemp seed moisture content $\leq$ 13.1% provided control	Tkalich, 1972
Bruchus rufimanus	28 mg/l	16 hrs at 16.7°C provided control	Roth and Richardson, 1974
Laspeyresia pomonella	32 g/m^3	2 hrs at 24°C provided control	Anthon et al., 1975
Pyrausta nubilalis	20 g/m^3	16 hr exposure provided control	
	16 g/m^3	24 hr exposure provided control	Isa et al., 1970
Termites	64 oz/950 ft^3	48 hr exposure provided control	Hicken, 1961
Curculio caryae	32 mg/l	24 hr, 100% kill in nuts with exit holes	
	80 mg/l	24 hr, 27°C, 100% kill in nuts with no exit holes	Leesch and Gillenwater, 1976
	112 mg/l	24 hr, 15°C, 100% kill in nuts with no exit holes	
Megastigmus aculeatus	50 g/m^3	24 hr exposure - complete kill	Vodolagin, 1971
Cadra cautilla	32 mg/l	killed larvae in shelled peanuts	
Plodia interpuncetella	32 mg/l	killed larvae in shelled peanuts	Leesch et al., 1974
Gnorimoschema operculella	11.74 mg/l	LD_{50} for larvae in potato tubers	Pradhan et al., 1960

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[a] Concentration - time

of oxygen consumption. When the LD_{50} (16 mg/l) was applied, those insects characterized by a high normal respiratory rate were more likely to be victims than those with low rates, suggesting that higher gaseous exchange rates enhance the toxicity of bromomethane. Respiration in the poisoned insects is not depressed until the organism is irreversibly paralyzed.

Winteringham (1956) monitored changes in the phosphate pool *in vivo* by studying effects of bromomethane on the ^{32}P-labelled pool in the adult housefly. In the poisoned insect, a depletion in the amount of ATP, but not ADP or AMP, was observed, as well as a decrease in the levels of glucose-6-phosphate following a 60-second exposure to bromomethane.

Sardesai (1972) reported that respiration was not inhibited in *Plodia interpunctella* following bromomethane poisoning. This supports the work by Bond (1956, 1975) cited previously. Examples of this phenomena can be seen in the work of Kenaga (1961) with *Tribolium confusum*; in Roth and Kennedy (1972) with *Anthoxomus grandis*; in Vincent and Lindgren (1975) with *Trogoderma variable*, and in Leesch and Gillenwater (1976) with *Curculio caryae*.

It appears that respiration (oxygen consumption) in bromomethane poisoned insects is not affected, but that changes in intercellular metabolic pathways may occur.

(iii) Resistance/Tolerance

Monro (1964) tested three species of insects (*Tribolium confusum*, *Tenebroides mauritanicus*, and *Sitophilus granarius*) for their tolerance to bromomethane. Only *Sitophilus granarius* developed a significant degree of tolerance. This developed tolerance carried over to other insecticides which were not chemically related to bromomethane (see Table 40). The tolerance

Table 40. Response to Fumigants of a Strain of Sitophilus granarius (London Wild at 27th selection) More Tolerant to Bromomethane Compared With Normal Nonselected Strain*

Dose in mg/l required for 50% mortality for 5 hr at 25°C

Fumigant	DOSE CH_3Br Tolerant	 Normal	Tolerance Ratio $\frac{CH_3Br\ Tolerant}{Normal}$
Methyl bromide	19.7	3.6	5.5
HCN	16.4	8.2	2.0
Acrylonitrile	4.9	1.05	4.7
Ethylene oxide	20.1	4.1	4.8
Chloropicrin	6.6	3.9	1.7
Phosphine	13.0	2.2	5.9
Ethylene dibromide	8.5	2.85	3.0

* Monro, 1964

developed by Sitophilus granarius indicates the development of a nonspecific system within the organism, which could have a wide utility in protecting it from potential pesticides.

Ellis (1972) selected 67 generations of Sitophilus granarius for their resistance to bromomethane. The individuals so selected were 1.3 times heavier than the nonselected. Subsequently, the two strains were exposed to 1,2-dibromomethane (EDB). The LC_{50} values for EDB were 2.75 ± 0.09 and 1.46 ± 0.05 ml/l, respectively, a 1.9-fold difference in tolerance.

Bond and Upitis (1972) found a strain of bromomethane tolerant Sitophilus granarius retained an appreciable level of tolerance for many years after bromomethane exposure was discontinued (see Table 41). Even after 16 years, the Montreal Wild strain, with an original 2.3-fold tolerance in 14 selections, still retained a 1.7-fold tolerance after 83 subsequent generations without bromomethane exposure.

Upitis et al. (1973), in a study of the genetic characteristics of a strain of Sitophilus granarius selected for tolerance to bromomethane, showed that the tolerance increased up to the 44th selection with a maximum of 7.8 times that of unselected insects. No increase was seen in the next six generations. Crosses between susceptible and selected strains yielded F_1 and F_2 hybrids which were intermediate in tolerance, with no change in the slope of the dose-response curves. This and the results of the F_1 back-cross hybrids were indicative of a polyfactional type of inheritance. Selected insects were heavier and had extended life cycles and lower respiratory rates that may have been related to increased tolerance. Table 42 summarizes these changes in the selected and nonselected strains.

Table 41. Tolerance of Selected Strains of Sitophilus granarius Adults to Bromomethane After Selection Pressure Was Removed (Dosage expressed as mg/l for a 5-hour exposure at 25°C.)[a]

Strain*	Maximum tolerance (LD$_{50}$ in mg/l. with SE)	No. generations after final selection	Years reared without selection	Present tolerance (LD)$_{50}$ in mg/l. with SE)
LW	3·6 ± 0·28	-	19·5	4·0 ± 0·48
LWANS	19·7 ± 0·97 (29)†	58	10·5	9·5 ± 0·45
LWA	28·2 ± 0·84 (50)	25	4·3	22·3 ± 0·32
GG	4·0 ± 0·32	-	16	4·5 ± 0·26
GGA	10·9 ± 0·41 (12)	68	12	7·3 ± 0·15
MW	4·3 ± 0·25	-	19·5	4·6
MWNS	9·3 ± 0·31 (14)	83	16	7·2 ± 0·13

* LW (London Wild) and MW (Montral Wild) are the original wild populations collected from field infestations. The letters A, NS, and ANS are designations given to selected strains for purposes of identity.

† Numbers in brackets refer to number of selections required to produce the level of tolerance indicated.

[a] Bond and Upitis, 1972

Table 42. Summary of Characteristics Affected by 44 Generations of Selection Imposed on *Sitophilus granarius* by Bromomethane*

Characteristic	Strain LWA (tolerant)	 LW (non-selected)
Body weight (mg)	3.6 ± 0.04	2.8 ± 0.02
Respiratory rate (µℓ O_2/g/hr	935 ± 5.9	1255 ± 26.7
life cycle (days)	44-48	34-36
LD_{50} (mg/ℓ)	28.2	7.8

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* Upitis *et al.*, 1973

From these studies on bromomethane, it appears that only a few insects have the genetic capability to adapt to this pesticide, and those that do appear to have a generalized mechanism which provides wide-range protection against a variety of pesticides. Subtle changes in insect morphology, such as weight gain, respiratory rate, and life cycle, all of which involve metabolic alterations discussed in the previous section, were apparent in these selected insects. Information on the other monohalomethanes was lacking.

(iv) Effects on Reproduction and Development

Howe and Hole (1966) noted that developing *Sitophilus granarius* were most susceptible to bromomethane on day 9 of development. Thereafter, susceptibility decreased up to 30 to 31 days of age (the early pupal stage), and then increased again. Eggs were about as susceptible as larvae of 23 days, but susceptibility increased with hatching. Free-living adults were slightly less susceptible than eggs and less susceptible than developmental stages outside the 28 to 32 day range. The developmental period of surviving individuals was apparently increased by the fumigation with bromomethane, and this lengthening of the developmental period is supported by Upitis *et al.* (1973). This increase in developmental period is accompanied by a decrease in respiratory rate and an increase in body weight.

b. Nematodes (Bromomethane Only)

The literature on the effects of bromomethane to nematodes is extensive, since bromomethane is primarily manufactured as a pesticide to control nematodes. Table 43 summarizes some data which are indicative of the effectiveness of bromomethane.

In addition to the above cited cases of bromomethane control of nematodes, Izutsuya (1973) states in a patent that a 500 ml solution of 3%

Table 43. Effects of Bromomethane on Nematodes

Nematode	Host	Effective Dose	Conditions	Other Effects	Source
Belonolaimus longicaudants *Trichoderus christiei* *Hemicycliophora parvana* *Hoploaimus tylenchiformis*	celery	871 lb/acre	98% MeBr 2% chloroprocin covered 48 hrs	also controlled nutgrass *Cyperus esculentas*	Darby *et al.*, 1962
Hoplolaimus columbus *Pratylenchus brachynrus* *Meloidogyne incognita*	cotton	954 g/40 cm pot	covered, aerated for 1 hr after 24 hrs	1 seedling per pot	Bird *et al.*, 1974
Anguina agrostis	bent grass	600-800 mg-hr/1	12% moisture	delayed germination of grass	Hague, 1963
Ditylenchus dipsaci	alfalfa seed	850 mg-hr/1	10-14% moisture	no effect on germination	Hague and Clark, 1959
Heterodera rostochiensis	potatoes	500-1000 mg-hr/1	---	100% kill	Hague, 1959
Meloidogyne javanica		200-300 lb/acre	chisel application, covered	killed at a depth of 3 feet	Thomason, 1959
Pratylenchus brachyurus	peanuts	24.5-50.9 mg/1	24 hr; 25°C in 1 ℓ flask	15% reduction in seed germination at 50.9 mg/1	Minton and Gillenwater, 1973
Pratylenchus thornei	wheat	487 kg/ha	covered following treatment for unspecified time	increased plant yield *decreased* grain yield	Van Gundy *et al.*, 1974
Pratylenchus penetrans	white clover	1 lb/sq ft	---	good control for 3 yrs post treatment	Chen *et al.*, 1962
Pratylenchus zeae	corn	2 lbs/100 sq ft	covered for 48 hrs following fumigation	increase in yield from 68.8 to 90.4 bushel/acre	Oakes *et al.*, 1956

Table 43. Effects of Bromomethane on Nematodes (Cont'd)

Nematode	Host	Effective Dose	Conditions	Other Effects	Source
Meloidogyne incognita acrita	sweet basil	150-200 lbs/acre	chisel applicator, covered or rolled and sprinkled	significant increase in yield	Sher *et al*., 1958
Meloidogyne javanica	tobacco	1 to 2 lbs/90 sq ft	98% MeBr and 2% chloropicrin covered, seed beds	also controlled rutgrass (*Cyperus rotundus*), black root rot (*Thielaviopsis basicola*), and anthracnose (*Colletotrichum tabacum*)	Milne, 1962
Heterodera trifolii	white clover	not stated	—	increase of 11.3% in yield	Yeates *et al*., 1975
Meloidogyne incognita	tomatoes, figs	600 ppm	38 hrs	became progressively less motile, but retained infectivity up to 38 hrs	Van Gundy *et al*., 1972
Xiphinema index	tomatoes, figs	600 ppm	28 hrs		
Dorylaimus sp.	tomatoes, figs	600 ppm	40 hrs		
Xiphinema index	grapevines	400-600 lb/acre	covered	good control for 4 years increased yields	Raski *et al*., 1975
Xiphinema americanum *Meloidogyne javanica* *Meloidogyne incognita* *Pratylenchus* sp.					
Xiphinema index *Meloidogyne incognita* *Heterodera schachtii* *Paratylenchus* sp.	figs tomatoes sugarbeets carnations	50-530 ppm 150-650 ppm 130-7670 ppm 1250-2500 ppm	21 days - 1 day 21 days - 1 day 21 days - 1 day 3 days - 1 day	sealed container	Abdalla and Lear, 1975
Heterodera rostochienis	potatoes	111 gm/m^2	covered 16 days 98% methyl bromide and 2% chloropicrin	increased yields increased nematodes	Whitehead *et al*., 1972

Table 43. Effects of Bromomethane on Nematodes (Cont'd)

Nematode	Host	Effective Dose	Conditions	Other Effects	Source
Meloidogyne sp.	roses	50 g/m^2	manure applied prior to fumigation decreased nematocidal effect	---	Scotto laMassese, 1973

bromomethane in kerosene applied to the surface of a pine tree (1 m^2) kills 100% of the nematodes infesting the tree within three days of application.

Overman (1968), in a six-year study, was unable to demonstrate any resistance development in nematodes exposed to 3 lb/100 ft^2.

Information on the effects on insects of other monohalomethanes is lacking. The comparison between species in Table 43 is difficult, as often the temperature, time of exposure, moisture content of soil, and other factors which influence bromomethane toxicity in nematodes are not constant among studies.

c. Invertebrates Other Than Insects and Nematodes (Bromomethane Only)

(i) Acute Toxicity

The effects of bromomethane on several gastropods, arachnids, and protozoans have been reported and are summarized in Table 44. In general, the levels of bromomethane required to control these pests commonly associated with foodstuffs are less than those required to control either insects or nematodes. Lethal exposures ranged from 5 mg/l for the protozoan Eimeria sp. to 240 mg/l for the gastropod Helicella sp.

(ii) Effects on Development

Working with Acarus siro, Boczek et al. (1975) isolated three periods of increased sensitivity to bromomethane. These were: (1) before the beginning of gastrulation movements in the germ band; (2) during the formation of the central nervous system; and (3) the period preceding dorsal closure. The first and third periods were described as periods of sensitivity in Tetranychus urticae by Krzysztofowicz and Boczek (1970). The work by Lewis (1948) may be used to help explain the periods of sensitivity. Recalling from Section III-B-1-d

Table 44. Effects of Bromomethane Fumigation on Gastropods, Arachnids, and Protozoans

Invertebrate	Dosage	Conditions/Results	Source
Gastropods			
Helicella candidula	240 mg/l	24 hr exposure, 100% mortality	Roth and Kennedy, 1973
Helicella conspurcata	240 mg/l	24 hr exposure, 100% mortality	
Cochlicella barbara	8 lbs/1000 ft^3	72 hr exposure, 55°F provided control	Richardson and Roth, 1965
Theba pisana	6 lbs/1000 ft^3	10 hr exposure, 55°F provided control	
Arachnids			
Rhipicephalus sanguineus	64 mg/l	3.5 hr exposure, 22.2°C provided control	Roth, 1973
	96 mg/l	6 hr exposure, 11.1°C provided control	
Acarus siro	21.2 mg/l	4 hr exposure, 22-24°C, 85% relative humidity provided control	Bednarek and Kuzitowica, 1970
	17.0 mg/l	8 hr exposure, 22-24°C, 85% relative humidity provided control	
	13.5 mg/l	16 hr exposure, 22-24°C, 85% relative humidity provided control	
	10.2 mg/l	24 hr exposure, 22-24°C, 85% relative humidity provided control	
Acarus siro	16.8 mg/l	4 hr exposure, 60°F, 85% relative humidity provided control	Burkholder, 1966
	8.1 mg/l	8 hr exposure, 60°F, 85% relative humidity provided control	
	5.2 mg/l	16 hr exposure, 60°F, 85% relative humidity provided control	
	3.4 mg/l	24 hr exposure, 60°F, 85% relative humidity provided control	
Tyrophagus lintneri	3 lbs/1000 ft^3	provided control	Stoller, 1962
Protozoans			
Eimeria tenella	5 mg/l	20 hr exposure, 25°C, destroyed oocysts	Long *et al.*, 1972
Eimeria acervulina	5 mg/l	20 hr exposure, 25°C, destroyed oocysts	

that bromomethane is absorbed by proteins with SH groups, and that the reaction is thought to be:

$$\text{R-SH} + \text{CH}_3\text{Br} \longrightarrow \text{R-SCH}_3 + \text{HBr}$$

Boczek et al. (1975) propose that if the toxicity of bromomethane is related to its ability to inactivate enzymes with SH groups, then the process of combining two SH groups would be inhibited. It is known that enzymes and other proteins containing sulfhydryl groups become active during the final stages of cleavage, at about the time of morphogenetic movements (Balinsky, 1975). The cells are dynamic and constantly changing shapes, forming many microtubules to assist in the movement. These microtubules consist mainly of proteins with an abundance of SH groups (Fulton and Klein, 1976).

Boczek et al. (1975) did not investigate the ultrastructure of the cell at the period of dorsal closure, but current understanding of morphogenetic movements suggests that microtubules containing proteins with SH groups could play a major role during dorsal closure.

Other areas for a potential source of inhibition do exist. Hexokinase activity, which is depressed by bromomethane (Dixon and Needham, 1946) and is present in the central nervous system, could affect the closure by inhibiting carbohydrate metabolism. Additionally, Lewis (1948) pointed out that papain, urease, and respiratory enzymes are also inhibited by bromomethane, any or all of which could affect embryonic development.

The results of these embryonic studies conducted in invertebrates could be applied to other developing organisms. Microtubular assisted morphogenetic movements and sulfhydryl containing compounds are common to all developing organisms. This area of embryonic effects of bromomethane, indeed all the monohalomethanes, presents an area on which more data are needed. The effects suggested by these studies on the failure of the nerve cord to close and the inhibition of morphogenetic movements should be evaluated in higher organisms.

5. Effects on Plants

a. Phytotoxicity

Most of the available information on phytotoxicity concerns bromomethane. This compound is often applied as a fumigant directly to plant seeds, plant cuttings, or harvested plant products and functions as a disinfectant during transportation or storage. In addition, bromomethane is used as a soil fumigant to control certain plant pests or undesirable plant species in cultivated areas. Most of the available phytotoxicity studies focus on establishing the most effective treatment conditions for these applications and are of limited use in assessing the effects of long-term, low-level exposure.

(i) Seed Fumigation

When bromomethane is applied directly to seeds as a fumigant, decreased germination may result. A number of factors may affect the severity of this response. As indicated in Table 45, the extent of germination reduction is positively correlated with the dose of bromomethane used and the moisture content of the seeds. Increasing fumigation temperature also enhances bromomethane phytotoxicity (Cobb, 1958; Strong and Lindgren, 1961). However, neither germination temperature (Powell, 1975a,b) nor oil content of the seeds (Blackith and Lubatti, 1960) seems to markedly affect the response of seeds to bromomethane injury. The period of storage after treatment may affect subsequent seed germination. Both Cobb (1958) and Lubatti and Blackith (1957) found that increased storage periods resulted in decreased germination. This could, in part, be related to residual bromomethane in seed batches. Roth (1972) noted that bromomethane dissipated relatively slowly from treated pine seeds and that high levels of bromomethane remained in the center of 45 kg bags of seed. This resulted in a substantial decrease in germination by seeds taken from the center of the bags.

Table 45. Effects on Germination of Seeds Fumigated with Bromomethane

Seed	Fumigation Conditions	Germination Results	Source
Hemp	70-140 g/m^3	5-23% reduction	Tkalich (1974)
Onion	1000 mg-hour/liter	95% reduction in lab 11.5% reduction in cool soil	Powell (1975b)
Peanuts a) paper container b) burlap bags	32 mg/liter (24 hr, 27°C, 80% relative humidity), applied under cover; aerated 72 hours	Reduction of: a) 21.7% in paper containers b) 11.4% in burlap bags	Leesch et al. (1974)
Oat, wheat, rye, barley	0, 600, or 1200 mg-hour/liter at 8, 11, 14, or 18% moisture content	At 18% moisture content: - no germination after 6 years storage - after 3 years storage, 80% wheat germinated At 8% moisture content: - 90% germination after 6 years storage[a]	Blackith and Lubatti (1965)
Picea abies, Picea glauca, Pinus mugo mughus, Pinus sylvestris (pine seeds)	Seeds at various moisture content; 48 g/m^3, 24°C, 2-5 hours; then aerated 1-24 hours and stored in sealed containers at 7° for 1 year	Germination normal after storage only if seeds aerated 24 hours before storage; all but P. sylvestris required drying to 5% m/c before storage	Jones (1968)
Tobacco seed	1-2 lb/1000 cu ft 48 hours or 2-3 lb/1000 cu ft 24 hours	Germination satisfactory at <10% seed moisture content: germination decreased at seed moisture contents above 10%	Guthrie and Kincaid (1957)
Barley, corn, grain sorghum, oats, wheat	<2 lb/1000 cu ft (<24 hours, 80°F); seed moisture content less than 12%	Unimpaired germination	Whitney et al. (1958)

[a] Except rye, germinated well only up to 3 years storage.

In situations where extended storage is necessary, refumigation is often required to retard microbial spoilage and insect infestations. Cobb (1958) and Kamel et al. (1973) both state the possibility that under some conditions the initial fumigation may cause changes in seeds making them more susceptible to damage by repeated fumigation. Kamel et al. (1973) found that by the third fumigation, corn seed germination was reduced to almost half of that of controls, while wheat decreased by 75% on the second fumigation. In addition, Cobb (1958) demonstrated the rapid and progressive deleterious effect of refumigation in combination with lengthening exposure to bromomethane. Conversely, Kempton and Maw (1972) found that germination of lettuce seeds planted in soils fumigated with bromomethane at a dosage of 1-2 lbs/100 sq. ft. is insensitive to the presence of inorganic bromide (the soil breakdown product of bromomethane).

(ii) Fumigation of Plants or Plant Products

Direct fumigation of plants or plant products by bromomethane is generally undertaken to retard pest infestations. It has been recommended for the control of cigarette beetles and tobacco moths on tobacco (Tenhet, 1957) and for reducing microbial spoilage on mango fruits (Subramanyam et al., 1969). Bromomethane fumigation of tomatoes promotes further damage of unsound fruit and slow colon development, as well as skin blotchiness (Akamine and Shojif, 1960). On the other hand, Junaid and Nasir (1955) stated that bromomethane-fumigated date cubes suffer no damage in quality or taste; a dosage of 35.5 mg/l (1 1/2 hour, 81°F) is sufficient for complete eradication of the insect pests *Oniyzaephilus* sp. and *Ephestia* sp. They also report that carnation cuttings suffered no damage at the same fumigant dosages that produced petal droop and withering of roses and tulips.

Iodomethane has received some consideration as a plant fumigant. Speitel and Siegel (1975) have determined that this compound does not induce abscission of petioles in Coelus plants as well as does iodine vapors (6/24 vs. 19/24). Likewise, iodomethane vapors have no effect on banana ripening 120 hours after treatment, whereas iodine vapors cause green bananas to turn either yellow or black. Thus, iodomethane probably presents little potential value as a fumigant.

(iii) Soil Application

The adverse effects on a number of flowering plants produced by soil fumigation by bromomethane have been evaluated. Roses show no pronounced toxic effects when planted in soils aerated for four days after bromomethane fumigation. However, carnations are extremely sensitive to both residual bromomethane gas and inorganic bromide in the soil (Malkomes, 1972; Coosemans, 1974). Lowering soil bromide levels by pre-treatment incorporation of peat and post-treatment flooding with water is effective in reducing the phytotoxicity of bromomethane- treated soils to carnations (Kempton and Maw, 1974). Cuttings of certain chrysanthemums are also highly susceptible to bromomethane damage. However, Gostick and Powell (1971) found marked differences in the sensitivity of varieties within different species of chrysanthemums when exposed to bromomethane-fumigated soils. In addition, Overman and Raulston (1972) demonstrated that bromomethane soil fumigation aggravates the phytotoxicity of Mocap - a soil nematocide - to chrysanthemum cuttings.

Soil fumigation may also adversely affect certain commercial crops. Lo (1967) found that sugarcane seedlings can survive in bromomethane-treated soil only if treated soils are aerated for up to sixteen days. Citrus seedlings also exhibit stunted growth on bromomethane-fumigated soils. However, stunting was related to decreased soil phosphorous caused by fumigation, rather than residual bromomethane or inorganic bromide (Tucker and Anderson, 1974). Certain tomato varieties seem relatively resistant to bromomethane soil fumigation (Volin and McMillian, 1974). Soil fumigation is also effective against a number of weeds, including: witchweed (Langston and Eplee, 1974), torpedo grass (Ryan and Kretchman, 1963), *Equisetum arvense* (Molin and Teär, 1957), *Oxalis latifolia* (Preest, 1964), *Cyperus rotundus* (Cristinzio *et al.*, 1973), *Cyperus esculentus* (Darby *et al.*, 1962), and to goose grass, rough bedstraw, crab grass, yellow neet sedge, annual sedge, spurge, and blue toad flax in holly nursery soils (Haasis and Sasser, 1962).

By injecting bromomethane into the soil around the base of healthy oak trees, bromomethane has been used to kill roots and thus prevent the spread of oak wilt disease (Himelick and Fox, 1961).

b. Beneficial Effects

In protecting plants against a variety of pests, bromomethane fumigation has been shown to increase growth rate, increase crop yields, and improve plant morphology. Studies on the positive results of bromomethane fumigation are summarized in Table 46.

c. Metabolic Effects

Bromomethane has been shown to cause a number of biochemical or physiological alterations in plants (Table 47). Direct fumigation of groundnuts inhibits respiration and catalase activity and results in decreased levels of nonreducing sugars and starch with increased levels of free fatty acids (Swamy, 1973). The breakdown of proteins is also decreased by such fumigation

Table 46. Results of Bromomethane Soil Fumigation on Growth and Yield of Various Seeds and Plants

Plant	Growth	Yield	Source
Corn (Coker 67 hybrid)	n.d.	+	Chapman (1962)
Cereal seeds	0	0	Lubatti and Blackith (1957)
Wheat and barley seeds	0/-	n.d.	Polchaninova and Sosedov (1972)
Alfalfa seeds	n.d.	0	Page *et al*. (1959)
Lima beans	n.d.	+	Madamba *et al*. (1967)
Cowpeas	n.d.	+	Madamba *et al*. (1967)
Okra	n.d.	+	Madamba *et al*. (1967)
Soybeans	+	+	Endo and Sasser (1958)
Celery	n.d.	+	Darby *et al*. (1962)
Carrots	+	+	Peachey and Winslow (1962)
Corn (Pioneer 3369A)	+	+	Grau *et al*. (1976)
Mushrooms	+	+	Tunney (1972)
Strawberries	n.d.	+	Wilhelm *et al*. (1974)
Head lettuce	n.d.	+	Wilhelm *et al*. (1974)
Snap canning beans	n.d.	+	Wilhelm *et al*. (1974)
Potatoes	n.d.	+	Wilhelm *et al*. (1974)
Huia white clover	n.d.	+	Yeates *et al*. (1975)
Carnation (La Rève Salmon Sim)	+	+	Coosemans (1974)
Eucalyptus saligna	+	n.d.	Veiga (1968)
Forest seedlings	+	n.d.	Molin and Teär (1957)
Pine seedlings	+	n.d.	Palmer and Hacskaylo (1958)
Ponderosa pine seedlings	+	n.d.	Peterson (1970)
Loblolly pine seedlings	+	n.d.	Hansbrough and Hollis (1957)
Holly (*Ilex crenata*)	+	n.d.	Haasis and Sasser (1962)
Spruce seeds	+	n.d.	Ingestad and Molin (1960)
Eucalyptus seedlings	+	n.d.	Magnani (1966)
Citrus aurantuim	+	n.d.	Cohn *et al*. (1968)
Citrus limettioides	+	n.d.	Cohn *et al*. (1968)
Pinus ponderosa scopulorum	+	n.d.	Weihing *et al*. (1961)
Pinus nigraaustciaca	+	n.d.	Weihing *et al*. (1961)

Key: + = increase; - = decrease; 0 = no change; n.d. = not determined.

Table 47. Metabolic Alterations Resulting from Bromomethane Fumigation of Plants and Seeds

Plant	Conditions	Result	Source
Almond meal Nut meal Pine-seed meal	Chamber fumigation	Thiamine content decreased; riboflavin content only slightly decreased	Siesto (1955)
Kafin corn	Fumigated and stored 2 months (airtight)	Decreased fatty acids, water soluble acids, reducing sugars, and amino nitrogen	Srinivasan and Majumder (1961)
Sesame seeds	Fumigation in holds of ships	Lower iodine and thiocyanate	Ratanova *et al*. (1962)
Alfalfa Silage	Chamber fumigation	Lactic acid and acetic acid buildup much less than untreated silage	Ionov (1968)
Citrus aurantium Citrus limettioides	Soil fumigation	Abnormal accumulation of Nain seedling leaves	Cohn *et al*. (1968)
Sunflower seeds	Chamber fumigation	Decreased respiration, reduced iodine and thiocyanate content	Kopeikovskii and Ryazantseva (1970)
Groundnuts	Chamber fumigation	Significant inhibition of respiration and catalase activity; lowered nonreducing sugars and starch, increased fatty acid accumulation	Swamy (1973)
Groundnut seeds	Chamber fumigation	Abnormally slow decrease of soluble and insoluble nitrogen in embryonic axis and cotyledons - due to proteolytic enzyme activity	Swamy and Reddy (1974)
Cocoa beans	Chamber fumigation	Bromomethane degrades in shells w/alcohol-insoluble proteins; methyl group binds with α-NH_2 of amino acid residues to imidazole rings of histidine and ϵ-NH_2 of lysine	Asante-Poku *et al*. (1974)

(Swamy and Reddy, 1974). Fumigation of stored alfalfa with bromomethane results in decreased levels of lactic acid and acetic acid (Ionov, 1968). In both sunflower seeds and sesame seeds, bromomethane fumigation was associated with decreased levels of iodine and thiocyanate (Ratanova et al., 1962; Kopeikovskii and Ryazantseva, 1970). In almonds, nuts, and pine seed meal, bromomethane treatment resulted in dose-related decreases in riboflavin levels but decreased thiamine levels only at lower bromomethane doses (Siesto, 1955). Abnormal accumulation of sodium has been noted in citrus seedling leaves grown in soil fumigated with bromomethane (Cohn et al., 1968). The direct relationship of any of these effects to gross signs of bromomethane phytotoxicity has not been elucidated.

d. Uptake and Distribution

A number of studies have attempted to determine the uptake and distribution of bromomethane in plants. Kempton and Maw (1972, 1973, 1974) demonstrated that bromide levels in carnations, tomatoes, and lettuce were directly related to elevated soil bromide levels caused by bromomethane fumigation. Similar results showing a correlation between bromomethane soil fumigation and plant bromide levels have been obtained using wheat and potatoes (Brown and Jenkinson, 1971; Brown et al., 1974). In both tomato plants and carnations, levels of inorganic bromide tended to decrease from the base to the tip of the plant (Kempton and Maw, 1973 and 1974). In tomato plants, leaves tend to concentrate greater amounts of bromide than the tomatoes (Kempton and Maw, 1973). In potatoes, Brown and coworkers (1974) found the greatest accumulation of bromide in the stems and stalks, while Scotto la Massese and Mars (1975) noted the highest levels of bromide in the potato skin. In cocoa beans, the methyl group of bromomethane apparently forms covalent bonds with protein amino groups, and such residues are found primarily in the alcohol insoluble shell proteins (Asante-Poku *et al*., 1974).

Using ^{131}I, Ohmomo and Saiki (1971) found that iodide levels were ten times greater than iodomethane levels in the leaves of Chinese cabbage, spinach, and camellia. No pronounced differences in uptake levels were noted among the three plants.

6. Effects on Microorganisms

a. Fungi (Bromomethane Only)

(i) General Use as a Fumigant

Much higher concentration-time (c.t.) products of bromomethane are required to kill fungi than are required to control insect and nematode pests. Generally speaking, susceptibility to bromomethane increases with increasing temperature.

In a study with two Australian forest soils treated with 244 g/m^2 of bromomethane (98% plus 2% chloropicrin), Ridge and Theodorou (1972) found that fungal recolonization was rapid, but original numbers were not obtained even 7 months after fumigation. Some fungi not detected in untreated soil colonized the fumigated soil. Seedling pine roots were always colonized by larger numbers of fungal species and organisms in the control soil than in the treated soil.

Munnecke *et al*. (1971) have reported that damping-off of peas caused by *Phthium ultimum* is best controlled in moderately moist soil (12%), with continuous bromomethane fumigation at approximately 2,500 ppm for 1 day or 1,650 ppm for 2 days. A 5-day exposure of 1,100 ppm or an 8-day exposure of 1,000 ppm also gives complete control. With *Rhizoctonia solani*, a 5-day exposure of approximately 2,100 ppm and an 8-day exposure of approximately 1,400 ppm would be required to prevent damping-off of peas.

Ohr *et al*. (1973) have reported the effects of sublethal bromomethane fumigation of citrus roots infested with *Armellaria mellea* and their subsequent storage in either sterile or nonsterile soil. *A. mellea* did not survive in nonsterile soil but did in sterile. Isolations of *Trichoderma* sp.

from the roots reached a maximum after storage of 7 to 8 days in nonsterile soil, and then declined as A. mellea populations approached zero. The populations of the two fungi were directly correlated by in vitro experiments. Populations of Trichoderma were 1.9 to 2.3 times more resistant to bromomethane than was A. mellea.

The effects of bromomethane fumigation on a wide variety of fungi are summarized in Table 48.

(ii) Uses in Commercial Mushroom Industry

A controversy seems to exist regarding pest control of commercially grown mushrooms by bromomethane fumigation. Dough (1968) reported that bromomethane controlled the pests of cultivated mushrooms at a dosage of 20 ml/m^3 for 24 hours under a polyvinyl chloride film tent. The author states that mushroom production is increased; therefore, bromomethane fumigation of mushroom houses has great potential economic value. Dieleman-van Zaayen (1971), however, reported negative results following bromomethane fumigation. She states that virus diseased mycelia and the spawn of mushrooms were not controlled by bromomethane fumigation, and supported the continued use of steaming the mushroom houses followed by the treatment of the wood with sodium pentachlorophenate. Tunney (1972) supports the role of bromomethane fumigation as an alternative for after-crop pasturization of mushrooms for disease control. Control of disease was achieved with an application of 600 oz hr/1,000 ft^3 at a minimum temperature of 70°F. Hussey et al. (1962) and Hussey (1964) showed that a bromomethane application of 0.6 oz hr/ft^3 killed insects, nematodes, mites, and virus infected mushroom mycelium. Flegg (1968) reported that a c.t. product exceeding 0.9 oz hr/ft^3 killed Verticillium malthousei. Hayes (1969) showed that a c.t. product of 0.625 oz hr/ft^3 killed mushroom mycelium and spores,

Table 48. Effects of Bromomethane on Fungi

Fungi	Dosage	Conditions/Comments	Source
Fusarium oxysporum f. lycopersici	100 g/m^2	controlled fungi on tomatoes	Weststeijn, 1973
Phytophthora parasitica	1 lb/100 ft^2	98% bromomethane, 2% chloropicrin, controlled fungi on citrus trees	Grimm and Alexander, 1971
Fusarium sp.	3 lb/plot (12.5'x20')	covered 6 days, controlled disease in petunias	Weihing et al., 1971
Sclerotina sclerotiorum	50 g/m^2	covered 48 hrs, controlled fungi in tobacco	Hartill and Campbell, 1973
Endomycorrhizae	454 g/40 cm pot	no infection on cotton	Bird et al., 1974
Penicillium sp.	1.6 and 3.3 g/m^3	reduced infestation from 76.9 to 11.1 and to 6.7% respectively in pecans	Wells and Payne, 1975
Alternaria sp. Pestalotia sp. Monochaeta sp. Cladosporium sp. Fusarium sp. Phoma sp. Aspergillus sp.			
Plasmodiophora brassicae	478.2 kg/ha	complete control of club root disease in cabbage	Wemalajeewa, 1975
Sclerotium rolfsii	50 g/m^2	controlled fungi in iris	Kiewnick, 1968
Anguina tritia	40-80 g/m^3	controlled fungi in wheat	Romascu, 1973
Fusarium bulbigenum lycopersici Verticillium dahliae	45-60 g/m^2 45-60 g/m^2	controlled tomato wilt in greenhouse	Perrotta, 1968
Armillaria mellea	3000 ppm 500 ppm	LD_{95} was 1.6 days on citrus roots LD_{95} was 9.5 days on citrus roots	Munnecke et al., 1970
Armillaria mellea	2 lbs/100 ft^2	covered, kills fungi	Munnecke et al., 1968

Table 48. Effects of Bromomethane on Fungi (Cont'd)

Fungi	Dosage	Conditions/Comments	Source
Thielaviopsis basicola	50 g/m^2	controlled fungi on tobacco	Mounat and Hitier, 1959
Verticillium sp.	70 g/m^2	controlled fungi on tomatoes	Matta and Garibaldi, 1965
Armillaria mellea	400 lbs/acre	controlled fungi in vineyards	Kissler *et al*., 1973
Armillaria mellea *Trichoderma viride*	1000 ppm (1 to 12 days) 600-1200 ppm 2400 ppm	growth inhibited for 20 days continued to grow ceased to grow while fumigating, resumed immediately upon removal of gas	Munnecke *et al*., 1973
Byssochlalamys fuloa	60-120 mg/kg	controlled fungi in tapioca starch	Ito *et al*., 1972
Eumargarodes laivgi	0.5 lb/100 ft^2	---	Hitchcock, 1968
Fusarium oxysporum	75-100 g/m^2	---	Dzidzariya, 1972
Phytophthora capsici	40 g/m^2	controlled fungi on green peppers	Alfaro Moreno and Vegh, 1971
Plasmodiophora brassicae *Rhizoctonia solani*	1-3 lbs/100 ft^2 1-3 lbs/100 ft^2	controlled fungi in cabbage	Winstead and Garriss, 1960
Orobanebe ramosa	0.5 lb/100 ft^2	controlled broomrape in tomatoes	Wilhelm *et al*., 1958
Fusarium oxysporum	125 g/m^2	controlled fungi on tomatoes	Vanachter, 1974
Rhizoctonia solani	125 g/m^2	controlled fungi in soil	
Pyrenochaeta lycopersici	125 g/m^2	controlled fungi in soil	
Aspergillus flavus	5 kg/m^3	5 day exposure controlled fungi in bee combs	Smirnov, 1970

irrespective of temperature, but that a minimum temperature of 19.4°C was critical in the destruction of *V. malthousei*. Hayes (1971), in giving recommendations for commercial fumigations, listed four requirements for success: a minimum exposure of 0.6 oz hr/ft^3; a concentration of 0.004 lb/ft^3 (64 g/m^3); a minimum air temperature of 21.1°C; and the removal of all large mushroom sporophores before fumigation.

b. Effects on Bacteria and Viruses (Bromomethane Only)

(i) General Use as a Fumigant

Bromomethane is used much less frequently as a bactericide than as an insecticide. *Salmonella pullorum* streaked on agar plates at 24°C and 100% relative humidity was killed by bromomethane fumigation at 2, 3, 4, and 5 lbs/1,000 ft^3 with 47, 44, 35, and 23-hour exposure, respectively (Maag and Schmittle, 1962). A relative humidity of 0, 50, or 100% within the fumigation chambers did not alter the activity of bromomethane at 5 lb/1,000 ft^3 in killing *S. pullorum* and *Staphylococcus aureus*. The inactivation rate of *S. pullorum* by bromomethane, when the percentage of survival was plotted against time, gave a curve essentially of an exponential character. Exposure of *S. pullorum* to 5 lb/1,000 ft^3 of bromomethane at 5, 24, and 32°C necessitated fumigation periods of 111, 23, and 11 hours, respectively, for a complete kill.

Inouye *et al*. (1967) and Doraiswamy *et al*. (1972) reported values of 640 g/m^3 and 200 g/m^3 (conditions unspecified) controlled tobacco mosaic virus. Van Winckel (1974) also reported that 200 g/m^3 controlled tobacco mosaic virus, while leaving sufficient fungi in the soil to degrade the virus.

Ridge (1976) has reported that, in a South Australian wheat field treated with a mixture of 200 kg/ha chloropicrin and 200 kg/ha bromomethane, the numbers of aerobic bacteria and fluorescent pseudomonads were greatly depressed. Within 10 days after fumigation, the numbers had risen sharply. For a further 14 days, the fluorescent pseudomonads formed the major portion of the aerobic bacterial population, and over five months later the bacterial population of the treated soil remained about 10 times higher than the control soil. Gram-staining randomly selected colonies showed that the treatment increased the percentage of Gram-negative organisms from 27% to 70%. Fluorescent pseudomonads are primarily associated with organic matter, and even though 97% are killed by the fumigation, the organic material provides excellent media for growth by the survivors.

A summary of the acute toxic effects of bromomethane on bacteria and viruses is presented in Table 49.

(ii) Metabolic Effects

Kolb and Schneiter (1950, cited in Hoffman, 1971) originally thought that the toxic action on bacteria of bromomethane was due to the hydrolysis of bromomethane in the cell to hydrobromic acid and methanol. Later, however, Kolb *et al*. (1952, cited in Hoffman, 1971) retracted this theory, just as mammalian toxicologists had, in favor of the concept that bromomethane itself disrupts the enzymatic structure or protein components of the cell. Later, researchers suggested that bromomethane reacts by alkylating the sulfhydryl, hydroxyl, carboxyl, and amino groups of macromolecules in the cell (Hoffman, 1971).

Recently, Colby *et al*. (1975) have presented evidence for an enzyme (bromomethane monooxygenase) in the bacterium *Methylomonas methanica* being responsible for methane oxidation *in vivo*. Extracts of *M. methanica* catalyze the O_2- and NAD(P)H-dependent disappearance of bromomethane.

Table 49. Effects of Bromomethane Fumigation on Bacteria and Viruses

Organism	Dosage	Conditions	Source
Vibro cholera *Shigella dysenteriae* *Salmonella typhi* *Salmonella paratyphi* A *Salmonella paratyphi* B	33 g/m^3	10 hr exposure provided control	Saiki, 1952 (in Harry *et al.*, 1972)
Corynebacterium sepedonicum	10% bromomethane, 5% ethylene oxide	18 hr exposure provided control	Richardson and Monro, 1962
Arabismosaic virus	2 lbs/ft^3	controlled virus on strawberry plants	Harrison *et al.*, 1963
Tobacco mosaic virus Cucumber green mottle virus	640 g/m^3 110 g/m^3 320 g/m^3	inactivate virus inactivate at 27°C inactivate at 14-16°C	Inouye *et al.*, 1967
Escherichia coli 1257	1000 mg/l	40°C and 90% relative humidity provided control	Prishchep and Nikiforova, 1969
Bacillus larvae *Bacillus alvei* *Bacillus paraalvei* *Streptococcus apis* *Streptococcus pluton* *Pseudomonas apisepticus*	5 kg/m^3	5 day exposure controlled bacteria in bee combs	Smirnov, 1970
Bacillus subtilis	bromomethane - 256 mg/l ethylene oxide - 160 mg/l	50 minute exposure provided control	Zych, 1971
Tobacco mosaic virus	200 g/m^3	inactivate virus in 3 Kg soil in which tomatoes were grown	Doraiswamy *et al.*, 1972
Salmonella typhimurium	800 mg-hr/l	25°C and 70% relative humidity provided control	Tucker *et al.*, 1974
Rhizoctonia violacea	50 g/m^2	eliminates bacteria from asparagus when applied to soil	Malot and Leroux, 1974
Xanthomonas begoniae	2 $lbs/100\ ft^3$	24 hr exposure eliminates bacterial blight from Rieger begonia	Strider, 1975

Bromomethane monooxidase is inhibited by metal-binding reagents, by other oxidase inhibitors (such as compounds SKF 525A and Lilly 53325), by some metal ions, and by acetylene. The optimum pH is 6.9. While this enzyme has as its normal function the oxidation of methane, its ability to metabolize bromomethane naturally should not be overlooked.

(iii) Effects on Microbial Interactions with Other Organisms

Musgrave *et al*. (1961) reported that bromomethane exerts selection pressure on a strain of grainary weevils (*Sitophilus granarius*). When a laboratory strain that is designated GG and dark brown in color is treated with bromomethane for several generations, the generations become tolerant to bromomethane and assume the light brown color characteristic of the MW strain that is resistant to bromomethane. Another characteristic of this MW strain is the lack of a rod shaped bacteria which is present in the mycetomes and female gonads of the GG strain. A study conducted on weevils of the GG strain which had undergone selection of controls for levels of mycetomal bacteria was undertaken. Of the 38 control individuals, all were positive for mycetomal microorganisms, and of the 60 organisms of the tolerant strain, all were negative. It therefore appears that the selected tolerance to bromomethane by the GG strain of grainary weevils is associated with the absence of the transformation of the mycetomal microorganisms.

McGaughey (1975) found that bromomethane was not compatible with the pathogens used to control the Indian meal moth (*Plodia interpunctella*). The pathogens, *Bacillus thuringiensis* and the granulosis virus, which are used to control the Indian meal moth, were either killed or their generation was prevented in the bacillus or inactivated in the virus.

(iv) Disinfecting Uses in the Poultry Industry

In a series of papers, Harry and coworkers (Harry et al., 1972; Harry et al., 1973; Harry and Brown, 1974) have discussed the role of bromomethane fumigation in controlling various microbes in poultry houses. At 25°C, a 20 hour exposure of various microorganisms found in the poultry house to bromomethane gas concentrations of 10 to 40 mg/l resulted in a marked reduction in the number of viable bacteria present, particularly, Salmonella typhimurium, Escherichia coli, enterococci, micrococci, and Aspergillus fumigants spores (Harry et al., 1972). However, no reduction was seen in dried Bacillus subtilus or in the E. coli phage. In finely sieved poultry house litter exposed to bromomethane under the same conditions as above, a marked reduction in the number of S. typhimurium, E. coli, and micrococci was observed. The activity of bromomethane was affected adversely by a reduction in temperature and by its application to litter with high moisture contents. Except in wet litter, a reduction of >99% of the S. typhimurium present resulted from exposure at 25°C to bromomethane concentrations as low as 10 mg/l; the microbe was undetected in samples exposed to 40 mg/l (Harry et al., 1973).

Harry and Brown (1974) conclude that bromomethane is useful as a fumigant in poultry houses at exposures of 100 to 800 mg-hr/l. Coccidial oocysts can be controlled by applications of 100 mg-hr/l, but exposures of 800 mg-hr/l are needed to control other pathogens.

(v) Effects on Rumen Bacteria

The presence of small amounts of halogenated methanes has been reported to inhibit lactic acid and pyruvic acid metabolism in rumen bacteria in sheep (Quaghebeur and Oyaert, 1971). Associated with this increasing inhibitory effect was a greater decrease in the acetic acid to propionic acid ratio. These authors conclude that iodomethane was taken up into transitory enzyme-substrate complexes which became stabilized in such a manner that their further entry into a reaction was stongly inhibited. Propionic acid is a necessary component in the ruminent's metabolism and, since these animals are dependent on the rumen bacteria for the production of this propionic acid, a chemical such as one of the monohalomethanes, which alters the acetic acid to propionic acid ratio, could have profound effects on the metabolism of both the bacteria and the ruminent ingesting the monohalomethane.

IV. REGULATIONS AND STANDARDS

A. Current Regulations

1. Bromomethane

a. Labelling Requirements

Under the Federal Insecticide, Fungicide and Rodenticide Act the required label statement for bromomethane included the skull and crossbones insignia and the word Poison. The following antidote and warning labellings were also required. "Antidote: Remove victim to fresh air immediately. Keep victim lying down and warm. Give artificial respiration if breathing has stopped. Call a physician immediately!" "Warning: Poisonous Liquid and Vapor! Contact with liquid may produce burns. Do not breathe vapor. Wear a full-face gas mask with black canister meeting specifications of the U.S. Bureau of Mines for organic vapors. Do not get in eyes, on skin or on clothing. In case of contact, immediately remove all contaminated clothing including shoes. Wash skin thoroughly with soap and water and flush eyes with water for at least 15 minutes. Get medical attention. Do not reuse shoes or clothing until free of all contamination" (Federal Register, 1962c).

b. Food Tolerances

The tolerance for residues of inorganic bromide resulting from fumigation with bromomethane was set at 200 ppm for almonds, brazil nuts, bush nuts, butternuts, cashew nuts, chestnuts, filberts, hazel nuts, hickory nuts, peanuts, pecans, pistachio nuts, and walnuts under the Federal Food, Drug and Cosmetic Act (Federal Register, 1957).

Additional tolerances under this act were listed in 1958 (Federal Register, 1958). A tolerance of 100 ppm was set for copra; 50 ppm was set for cipollini bulbs, garlic, peas with pods, sweet corn; 30 ppm was set for carrots, citrus citron, cucumbers, grapefruit, horseradish, Jerusalem artichokes, kumquats, lemons, limes, okra, oranges, parsnips (roots), peppers, pimentos, radishes, salsify roots, strawberries, sugar-beet, summer squash, tangelos, tangerines and yams; and 20 ppm was set for apricots, cantaloups, cherries, grapes, honeydew melons, mangoes, muskmelons, nectarines, papayas, peaches, pineapples, plums, pumpkins, watermelons, winter squash and zucchini squash.

Dried fruit residues allowable are 150 ppm in figs, 100 ppm in dates, 50 ppm in raisins, 30 ppm in apples, apricots, peaches and pears, and 20 ppm in prunes (Federal Register, 1960a). The residue of inorganic bromide permissible in popcorn is 240 ppm (Federal Register, 1960b).

Revisions to these initial lists of allowable inorganic bromide residues resulting from bromomethane fumigation include cabbage at 50 ppm (Federal Register, 1961); asparagus at 100 ppm (Federal Register, 1962a); avocados at 75 ppm (Federal Register, 1962b); dried eggs, processed herbs and spices at 200 ppm (Federal Register, 1964); soybeans at 200 ppm (Federal Register, 1965a); eggplants at 60 ppm, muskmelons and tomatoes at 40 ppm, broccoli, cauliflower, peppers, pineapples and strawberries at 25 ppm (Federal Register, 1965b). The muskmelon tolerance represents an increased tolerance level from 20 to 40 ppm and the pineapple from 20 to 25 ppm. However, tolerance levels for peppers and strawberries were decreased from 30 to 25 ppm.

The following inorganic bromide tolerances were established for food commodities fumigated with bromomethane, or with bromomethane and/or dibromomethane and/or 1,2-dibromo-3-chloropropane: in or on dog food, 400 ppm; in milled fractions of animals feed from barley, corn, grain sorghum (milo), oats, rice, rye, and wheat, 125 ppm; in parmesan and roquefort cheese, 325 ppm; in or on processed foods not elsewhere covered, 125 ppm. The previous tolerance of 50 ppm was increased to 125 ppm in milled fractions derived from cereal grains from all fumigated sources (Federal Register, 1966a). Tolerance in coffee beans was set at 75 ppm and in cumin seed and ginger root at 100 ppm (Federal Register, 1966b). Tolerances for dried eggs and processed herbs and spices were increased from 200 ppm to 400 ppm when the inorganic source of bromide was bromomethane alone, and the tolerances in or on flours of barley, corn, sorghum (milo), rice, rye and wheat were set at 125 ppm when the inorganic origin of bromide was both bromomethane and dibromomethane (Federal Register, 1966c).

Inorganic bromide residue tolerances resulting from fumigation with bromomethane were set at 50 ppm in timothy hay (Federal Register, 1967a). The total residue of inorganic bromide resulting from a fumigation of a mixture of bromomethane and dibromomethane was set at 125 ppm (Federal Register, 1967b). Finally, a residue of 100 ppm is allowed in pomegranates fumigated with bromomethane (Federal Register, 1972).

c. Standard for Human Exposure

In 1957, the Texas State Department of Health set a maximum of 20 ppm bromomethane exposure during an eight hour work day. They further stated that respirators protect for only two hours at bromomethane levels of 5 lbs/1000 ft^3. Therefore, all respirators should be destroyed after two hours use. After the seal is broken, the respirator should be destroyed in one year regardless of use and in two years from the date of purchase even if the seal is unbroken (Texas State Department of Health, 1957).

The American Conference of Governmental Industrial Hygienists established a TLV for bromomethane of 20 ppm at 25°C and 760 mm (Stokinger, 1963). This ceiling level is recommended to prevent serious neurotoxic effects and pulmonary edema (American Conference of Governmental Industrial Hygienists, 1971).

The American National Standards Institute, Inc. (1970) has set the following standards for bromomethane exposure. In a five minute period in an eight hour day not more than 50 ppm should be exceeded. The ceiling concentration for any eight hour day is 25 ppm and the time-weighted average for an eight hour day should not exceed 15 ppm. In selecting these standards, the Institute used the following criteria: avoidance of (1) undesirable changes in body structures or biochemistry; (2) undesirable functional reactions that have no discernible effects on health; and (3) irritation or other adverse sensory effects.

The 50 ppm concentration, for a duration of five minutes, is acceptable only if encountered not more than once in an eight hour work day and the 25 ppm ceiling and time-weighted average of 15 ppm are not exceeded.

Based on animal and human exposure data, the ceiling of 25 ppm was acceptable if the time-weighted average is at or below the 15 ppm level for an eight hour day. OSHA has set 20 ppm as the ceiling value for exposure to bromomethane (Federal Register, 1975). They note that significant absorption of bromomethane can occur via the skin.

2. Chloromethane

a. Labelling Requirements

Chloromethane is required to have the following labelling under the Federal Insecticide, Fungicide and Rodenticide Act. "Warning:

Flammable! May Be Fatal If Inhaled. Contact with liquid may produce burns. Do not breathe vapor. Do not get in eyes or on skin. Do not use or store near heat or open flame" (Federal Register, 1962c).

b. Food Tolerances

Chloromethane may be used under the Federal Food, Drug and Cosmetic Act as a propellant in pesticide formulations in an amount not to exceed 30% of the finished formulation, when used in food storage and processing areas where spray areas do not contact fatty foods (Federal Register, 1962d).

c. Standards for Human Exposure

Based on work in rats on chronic poisoning by chloromethane, a maximum permissible concentration of 5 mg/m^3 was established in industrial plants in Russia (Evtushenko, 1966). OSHA has set 100 ppm as the maximum acceptable eight hour time-weighted average exposure to chloromethane (Federal Register, 1975), which is also the level recommended by the American Conference of Governmental Industrial Hygienists (American Conference of Governmental Industrial Hygienists, 1971).

3. Iodomethane and Fluoromethane

No current regulations governing chloromethane or fluoromethane were found.

B. Current Handling Practices

1. Special Handling in Use

a. Fluoromethane

There are no specific practices or handling procedures for fluoromethane in the literature examined. As a gas, it is delivered and used under pressure, and the same procedures for handling all compressed gases in tanks would apply to fluoromethane. In addition, because not very much is known about the toxicity of fluoromethane, it should be handled in such a way as to avoid personal contact. It would be desirable also to restrict the escape of any excess or discarded fluoromethane to the environment.

b. Chloromethane

Handling practices for chloromethane are specified in the Chemical Safety Data Sheet SD-40 published by the Manufacturing Chemists Association (MCA, 1951).

Chloromethane is a toxic material whose inhalation symptoms may mimic inebriation. Serious symptoms sometimes do not appear until after repeated exposure or a latency period. Personnel working with or in the vicinity of chloromethane must therefore take strict precautions against contact with it. Safety goggles should be worn to avoid contact with the eyes. Respiratory protection should include masks and equipment of the type approved by the U.S. Bureau of Mines. The use of air lines, positive pressure masks, or self-contained breathing apparatus depends on the circumstances, facilities, and training of the personnel involved. Liquid chloromethane will penetrate leather gloves, shoes, and possibly other clothing. These items should be removed if in contact with liquid chloromethane and thoroughly dried and aired; then they may be reused.

Ventilation of enclosed areas where chloromethane is being used is essential to keep the concentration below the maximum allowed safe level. Because it is more dense than air, chloromethane tends to sink and collect at the lowest possible levels of the enclosed area.

Chloromethane is stored as a compressed gas or liquid under pressure. It burns only feebly, but forms explosive mixtures with air in the concentration range 8 to 17%. Flames, heat, friction, and static electricity must therefore be avoided when working with chloromethane. Chloromethane suspended in oil fogs from refrigerant units are especially explosive. Carbon dioxide satisfactorily smothers chloromethane fires.

c. Bromomethane

Procedures for handling bromomethane are given in the Manufacturing Chemists Association Safety Data Sheet SD-35 (MCA, 1968).

Bromomethane is often supplied in one pound cans for fumigation purposes. The cans should never be opened with an ordinary can opener, but must be handled with special equipment designed for fumigation.

Cylinders of bromomethane should be handled with the same precautions as cylinders of any other poisonous gas. Ordinary rubber clothing, including gloves and boots, is not satisfactory protection against bromomethane vapors or liquid. Leather shoes and plastic covered canvas gloves are recommended. Woolen outer clothing is considered satisfactory. All articles of clothing which come in contact with bromomethane should be removed and not reused until sufficiently ventilated to disperse all the bromomethane residue. Respiratory protection may be obtained from airline masks, positive pressure hose masks, self-contained breathing apparatus, or suitable industrial type gas masks capable of absorbing bromomethane. (The latter are not safe, however, for emergency spills where the concentrations of bromomethane are unknown and may be especially high, or in situations which may present insufficient oxygen.)

d. Iodomethane

Iodomethane liquid and vapor are toxic. Iodomethane can alkylate proteins (Heuser and Scudamore, 1968) and may possibly be carcinogenic. Adequate ventilation through the use of a good hood and avoidance of contact with the vapors are therefore essential to safe handling.

2. Storage and Transport Practices

Chloromethane is shipped in cylinders containing 70, 100, 145, or 300 pounds each (MCA, 1951). They are equipped with safety devices approved for this service and are filled to a maximum of 84% of their capacity. Single unit tank cars holding 40,000 or 78,000 pounds of chloromethane are also used for transport.

Cylinders must be protected in storage against extremes in temperature. Ordinary steel pressure tanks are suitable for storage of chloromethane if they are kept grounded to discharge static electricity. Storage areas should be away from heat sources or fire hazards. Natural ventilation is considered adequate for outdoor storage.

Bromomethane is stored and transported in metal cans in wooden or fibre board boxes. Tin-plated cans with concave pressure ends are used. Metal cylinders are employed for larger quantities. Tank car shipments are rare (MCA, 1968). All storage areas should be dry and cool. In some cases refrigeration is used to minimize evaporation and pressure in storage containers. Natural or mechanical ventilation should be provided to remove excessive concentrations of bromomethane which may leak from storage containers or piping.

Fluoromethanes are stored and transported in cylinders suitable for gases under pressure. Iodomethane is packaged for laboratory use in bottles or cans which are shipped in heavy cardboard cartons with foamed plastic or other suitable filling.

3. Accident Procedures

Because of the high volatility of the monohalomethanes, specific cleanup procedures in the event of accidental spills are neither necessary nor possible. Only iodomethane would persist in the liquid state for a short period of time following a spill, but no specific containment procedures were noted in the literature examined.

The greatest hazard presented by accidental spills of monohalomethanes is the possible poisoning of personnel in the vicinity of the accident by inhalation of the vapors. In the event of the accidental exposure of an individual to any of these chemicals, quick removal from exposure is the most important and primary procedure. The second hazard is fire or explosion, most likely with mixtures of chloromethane and air (bromomethane is a fire extinguishing agent). Hence, rapid, thorough ventilation of the spill area is essential. Because of the volatility of these compounds, adequate dilution with air in the event of an accident may be a major factor in avoiding or minimizing human exposure.

TECHNICAL SUMMARY

The monohalomethanes are colorless gases (fluoromethane, chloromethane, and bromomethane) and a liquid (iodomethane) with faint odors, slight solubility in water, and high solubility in nonpolar organic solvents.

Chloromethane, at about 411 million pounds annual production, is the most significant of the monohalomethanes from a commercial standpoint. The production of bromomethane is about 40 million pounds per year, and the production of iodomethane is approximately 20,000 pounds annually. Fluoromethane is not a commercially significant chemical.

Chloro-, bromo-, and iodomethanes are manufactured by the hydrohalogenation of methanol in processes which differ in detail according to the desired halogen in the end product. Direct halogenation of methane is no longer significant as a manufacturing process of monohalomethanes.

The sea is a natural source of all monohalomethanes except fluoromethane (Lovelock *et al.*, 1973). All except fluoromethane have been monitored in seawater (Lovelock *et al.*, 1973, and Lovelock, 1975) and in drinking water (Shackelford and Keith, 1976), in the latter case possibly as the result of disinfection by chlorination. Monohalomethanes have been monitored in the air over the oceans (Lovelock *et al.*, 1973, and Lovelock, 1975), as well as inland (Lillian and Singh, 1974, and Grimsrud and Rasmussen, 1975). Bromomethane has also been monitored in soil (after fumigation) (Kolbezen *et al.*, 1974), human food, and animal feed. Algae in the sea are believed to be the major natural origin of bromomethane and iodomethane, with chloromethane forming by the reaction of chloride ion in seawater with iodomethane (Zafiriou, 1975). Anthropogenic sources of monohalomethanes include slash and burn agriculture (chloromethane - Lovelock, 1975) and industrial processes, such as some plastics manufacturing, pesticide application, and soil fumigation. Wofsy et al. (1975) have suggested that 5 to 25% of the bromomethane in the atmosphere can be attributed to anthropogenic sources. In contrast, Lovelock (1975) has calculated that almost 100% of the chloromethane and iodomethane detected in the environment can be attributed to natural sources.

Commercially produced chloromethane is used mainly for the production of silicones and tetramethyl lead (a gasoline additive). Bromomethane is used principally as a fumigant for soil, enclosed areas, and food products. It is effective against a wide variety of pests and disease causing and carrying organisms. Iodomethane is used as a laboratory and commercial alkylating agent and in tungsten-halogen lamps; the latter use is shared with chloro- and bromomethane.

Nuclear fission reactors are a major potential source of environmental contamination with $CH_3{}^{131}I$, a radioactive (as well as chemical) hazard (Thompson and Kelley, 1975). Other processes which may result in the production of monohalomethanes in the environment include the breakdown of halogenated pesticides (Silk and Unger, 1972) and the combustion of gasoline containing halogenated molecules (Wofsy et al., 1975). However, most of the bromo-, chloro-, and iodomethanes detected in the environment are attributable to natural sources (Lovelock, 1975, and Wofsy et al., 1975).

In the sea, hydrolysis is the main mechanism for degradation of monohalomethanes. They hydrolyze slowly in water (Stenger and Atchison, 1964) to produce methanol and hydrogen halide. In the atmosphere, degradation is initiated by photolysis and reaction with hydroxyl radicals. Although data on persistence is limited, iodomethane appears to be the least stable of the four compounds, with an atmospheric half life of about two days (Singh et al., 1977). Stability of the monohalomethanes increases in the order: $CH_3I < CH_3Br < CH_3Cl < CH_3F$. The residence time for chloromethane in the troposphere is expected to be 0.37 years, based on reaction with hydroxyl radicals (Lovelock, 1975). Bromomethane should react about 10% slower (Robbins, 1976). The evidence suggests that persistence in the soil depends on depth of application, moisture content, soil type, temperature, and other factors (Kolbezen et al., 1974).

Monohalomethanes appear to have a low potential for bioconcentration; no data are available on biodegradability. Environmental transport is principally by evaporation from water and subsequent transport through air. Bromomethane and chloromethane are considered to be sufficiently stable in the troposphere to reach the stratosphere in significant quantities (Wofsy et al., 1975, and Robbins, 1976). The chlorine and bromine atoms introduced into the stratosphere by natural bromomethane and chloromethane may play some role in maintaining stratospheric ozone balance.

The monohalomethanes have been studied in many biological systems. Information on the toxic effects of bromomethane on numerous target organisms is extensive. However, the effects on man and experimental animals are limited primarily to studies involving acute exposures, with little information being available on biochemical or metabolic effects.

The symptoms of bromomethane poisoning in man are that of a substance causing a diffuse neurotoxic reaction. Most human exposures are the result of accidental poisonings during a fumigating process. Exposures are usually followed by a latent period of 30 minutes to 48 hours before symptoms develop.

Acute exposures to bromomethane of 100 ppm or less in humans have not been reported to cause permanent damage, while exposures of 135 ppm result in moderate disability. Exposures of 175 ppm result in slight residual ataxia; at 250 ppm convulsive seizures are seen, with death or permanent neurological changes resulting in some patients. Exposures of 400 ppm result in gross disability in survivors (Hine, 1969, and Rathus and Landy, 1961).

Exposures to chloromethane are usually the result of leaks in refrigerant systems. Neurological symptoms are the prominent symptoms evidenced in man and experimental animals. Complete recovery from chloromethane poisoning may take months and, in some cases, permanent changes in personality and central nervous system responses have been noted in persons repeatedly exposed at 25 to 10,000 ppm for up to several weeks duration (MacDonald, 1964). Acute exposure to 500 ppm will produce a syndrome of severe chloromethane poisoning.

Iodomethane exposure also expresses itself by causing changes in the central nervous system. However, dose-response data for acute effects in man are not known, but must be extrapolated from animal studies. Iodomethane is considered to be the most toxic of the monohalomethanes (von Oettingen, 1964).

The similarities in the toxicological responses to the monohalomethanes suggest a similar mode of action. The most probable mechanism is that the monohalomethane participates in the methylation of essential enzymes, cofactors, and intracellular proteins, thereby rendering them inactive. Sulfhydryl-containing groups seem particularly susceptible to the monohalomethanes (Lewis, 1948, and Redford-Ellis and Gowenlock, 1971a). Various reports on the effectiveness of cysteine administration in the treatment of monohalomethane poisoning support the contention that monohalomethanes inactivate sulfhydryl compounds (Mizyukova and Bakhisnev, 1971).

Studies on the biological effects of monohalomethanes in laboratory animals confirm and support the effects observed after human exposures. The compounds all produce central nervous system involvement and alterations in the metabolism of glutathione and other sulfhydryl compounds. Acute toxicity data confirm that iodomethane is more toxic than bromomethane which, in turn, is more toxic than chloromethane in all animals tested. For example, exposures of 72 ppm iodomethane, 150 ppm bromomethane, and 3,000 ppm chloromethane are lethal in mice (von Oettingen, 1964). Chronic studies with bromomethane and chloromethane indicate that daily exposures to 33 ppm bromomethane in rabbits and 500 ppm chloromethane in monkeys and dogs will eventually cause the same neurological changes as seen in acutely exposed animals.

Toxicological characteristics in animals, as in humans, have been demonstrated to be the result of monohalomethane interference with sulfhydryl-containing proteins. Several investigators have shown that the monohalomethanes interfere with glutathione metabolism (Redford-Ellis and Gowenlock, 1971 a, b; Boyland et al., 1961; Barnsley, 1964; Johnson, 1966; and Barnsley and Young, 1965). A possible pathway for chloromethane metabolism in the liver involving glutathione has been suggested by Redford-Ellis and Gowenlock (1971 a, b) and for iodomethane by Barnsley and Young (1965) (see Figure 13).

Chloromethane and iodomethane have both been reported to be mutagenic in the Ames assay (Andrews et al., 1976, and McCann et al., 1975). Injection of iodomethane has increased the incidence of lung adenomas in mice (Poirier et al., 1975), and subcutaneous injections cause local sarcomas in rats. Based on the available information, iodomethane possesses the greatest carcinogenic/mutagenic potential of the monohalomethanes.

Chickens exposed to chloromethane (2,000 ppm daily) developed abducted legs after three weeks of exposure and died after five to six weeks of exposure (Smith and von Oettingen, 1947a). No information is available on the effects of the monohalomethanes on fish or reptiles.

Bromomethane has been utilized successfully in the control of insects in numerous agricultural situations, in disinfection of cargo at ports of entry, and for the storage of processed foods. Residual bromide levels which are permitted in these foodstuffs range from 15 to 400 ppm, depending on the foodstuff, and are regulated by the FDA. Metabolic studies indicate that bromomethane toxicity in insects is correlated positively to the insects' rate of oxygen consumption (Bond, 1956, 1975). Further, a depletion in the amount of ATP, but not ADP or AMP, is observed in the poisoned insects (Winteringham, 1956). Tolerance to bromomethane has been demonstrated in only one species, *Sitophilus granarius* (Monro, 1964; Ellis, 1972; Bond and Upitis, 1972; and Upitis *et al*., 1973). After the 44th selection, the insect was 7.8 times more tolerant to bromomethane than the nonselected organisms. Iodomethane has been used only to a limited extent as an insecticide, while chloromethane has not been used at all.

Bromomethane controls nematodes effectively and is used extensively to protect a variety of crops, flowers, and trees from these pests. Bromomethane also effectively controls gastropods, arachnids, and protozoans. Bromomethane has been noted to affect the morphogenic movements in several species, resulting in malformed embryos (Boczek, 1975, and Krzysztofowicz and Boczek, 1970). While arachnid and mammalian development are not the same, many similarities exist, and the possibility of embryonic death or terata in mammalian species is suggested.

Bromomethane application may produce phytotoxicity in certain instances. There is some question as to how direct application to seeds may affect germination. Decreases in germination are associated with high moisture content and/or high temperatures (Cobb, 1958). When applied to the soil, bromomethane and the residual soil bromide may affect the plant. Carnations and chrysanthemums are particularly susceptible to bromomethane damage. Commercial crops, such as sugar cane or citrus seedlings, may be stunted if the soil is not well aerated after fumigation. However, bromomethane protects plants from pests and increases growth rate and yield in most instances when applied properly.

Fungi can be controlled by bromomethane, but at higher concentration-time products than are required to control insects or nematodes. Bromomethane has been used to control pests found in mushroom houses. Bromomethane is not a widely used bactericide, but controls various microbes in poultry houses. It also is effective against the tobacco mosaic virus and several other microbes of commercial importance. The bacterium *Methylomonas methanica* possesses an O_2- and NAD(P)H-dependent enzyme (bromomethane monooxygenase) capable of metabolizing bromomethane (Colby *et al.*, 1975).

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CONCLUSIONS AND RECOMMENDATIONS

The monohalomethanes represent an unusual quartet for a review of this type. Their physical, chemical, and biological properties are related as anticipated by the Periodic Law, but from a commercial point of view they are four distinct and totally unique materials which have little in common other than some minor uses.

Chloromethane is by far the most industrially significant of the monohalomethanes. It would be natural to focus on this compound in terms of setting standards for human exposure and exploring the consequences of its ubiquity in the environment, especially its potential effect on the stratosphere, if, indeed, chloromethane is eventually detected in the stratosphere. However, it appears that opportunities for escape of anthropogenic chloromethane to the environment are minimal since more than 90% of it is used to synthesize other chemicals and therefore is not available to contaminate the environment.

Although the production of bromomethane is only about 10% of that of chloromethane, practically all the bromomethane produced is released to the environment from its use as a fumigant, posing a distinct hazard to applicators and occasionally to others. Bromomethane does not persist very long in well-ventilated areas; its decomposition products are inorganic bromides. Even though considerable amounts of bromomethane are released to the environment, the quantity is considered to be small (5-25%) compared to natural sources.

Iodomethane is used in relatively small quantities in industry compared to chloro- and bromomethanes. The amount of iodomethane released to the environment is insignificant compared to its natural sources.

Fluoromethane has no significant commercial uses. It is strictly a research chemical at the present time and is likely to remain so in the future. It is difficult and expensive to make in pure form.

Practically nothing is known about the toxicity and environmental effects of fluoromethane, and the quantities produced and used do not suggest a high priority for obtaining such information. The other monohalomethanes are all alkylating agents to some degree, and iodomethane and chloromethane appear to be mutagenic/carcinogenic. Alkylation of essential enzymes appears to be the common mode of toxic action; neurological symptoms resulting from exposure have been noted in both man and animals. Very little information is available on chronic doses and considerably more work is necessary, especially from an occupational safety standpoint, tc determine adverse as well as no-effect levels.

Very little ecological effects information is available except for the action of bromomethane on target organisms. Because these compounds are natural products, more data in this area would be of academic interest.

All of the monohalomethanes (except fluoromethane) are natural products, found in considerable abundance in seawater and the troposphere. In setting standards for permissible levels of monohalomethanes released from chemical processess, it will be necessary to have background data and possess knowledge of the probable effects, if any, of additional environmental loading. Thus, research to obtain a more complete chemical picture of the natural monohalomethane cycles: origins, lifetimes, and fates seems warranted.